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FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005

=> d his

     (FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
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FILE 'LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
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=> s proteinase? or protease?
L1      620411 PROTEINASE? OR PROTEASE?

=> s serine
L2      394137 SERINE

=> s l1 and l2
L3      104666 L1 AND L2

=> s "HELA2"
L4            9 "HELA2"

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            6 DUP REM L4 (3 DUPLICATES REMOVED)

=> d 1-6 ibib ab

L5   ANSWER 1 OF 6  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:   2003:542323  BIOSIS
DOCUMENT NUMBER:    PREV200300544975
TITLE:              Synthesis and antitumor activity of N-sulfonyl derivatives
                    of nucleobases and sulfonamido nucleoside derivatives.
AUTHOR(S):          Zinic, B. [Reprint Author]; Krizmanic, I.; Glavas-Obrovac,
                    Lj.; Karner, I.; Zinic, M.
CORPORATE SOURCE:   Ruder Boskovic Institute, Bijenicka 54, 10 000, Zagreb,
                    Croatia
                    bzinic@rudjer.irb.hr
SOURCE:             Nucleosides Nucleotides & Nucleic Acids, (May-August 2003)
                    Vol. 22, No. 5-8, pp. 1623-1625. print.
                    ISSN: 1525-7770 (ISSN print).
DOCUMENT TYPE:      Article
```

LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003

AB The introduction of sulfonamido group on the C-2 position of pyrimidine nucleosides was achieved by ring opening of 2,2'- and 2,3-anhydronucleosides. N-sulfonyl derivatives of nucleobases and sulfonamido derivatives of nucleosides Were assayed for in vitro antitumor activity.

L5 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:303061 BIOSIS
DOCUMENT NUMBER: PREV200300303061
TITLE: TRF1 is degraded by ubiquitin-mediated proteolysis after release from telomeres.
AUTHOR(S): Chang, William; Dynek, Jasmin N.; Smith, Susan [Reprint Author]
CORPORATE SOURCE: Skirball Institute of Biomolecular Medicine, New York University School of Medicine, New York, NY, 10016, USA
smithsu@saturn.med.nyu.edu
SOURCE: Genes & Development, (June 1 2003) Vol. 17, No. 11, pp. 1328-1333. print.
CODEN: GEDEEP. ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jul 2003
Last Updated on STN: 2 Jul 2003

AB Mammalian telomeres are coated by the sequence-specific, DNA-binding protein, TRF1, a negative regulator of telomere length. Previous results showed that ADP-ribosylation of TRF1 by tankyrase 1 released TRF1 from telomeres and promoted telomere elongation. We now show that loss of TRF1 from telomeres results in ubiquitination and degradation of TRF1 by the proteasome and that degradation is required to keep TRF1 off telomeres. Ubiquitination of TRF1 is regulated by its telomere-binding status; only the telomere-unbound form of TRF1 is ubiquitinated. Our findings suggest a novel mechanism of sequential posttranslational modification of TRF1 (ADP-ribosylation and ubiquitination) for regulating access of telomerase to telomeres.

L5 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:42593 BIOSIS
DOCUMENT NUMBER: PREV200300042593
TITLE: DNA molecules encoding human **HELA2** or testisin serine proteinases.
AUTHOR(S): Antalis, Toni Marie [Inventor, Reprint Author]; Hooper, John David [Inventor]
CORPORATE SOURCE: Toowong, Australia
ASSIGNEE: Amrad Operations Pty., Ltd., Victoria, Australia
PATENT INFORMATION: US 6479274 20021112
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 12 2002) Vol. 1264, No. 2.
http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB The present invention related generally to novel molecules and more particularly novel proteinaceous molecules involved in or associated with regulation of cell activities and/or viability. The present invention is particularly directed to novel serine proteinases and a novel kinase and to derivatives, agonists and antagonists thereof. In one embodiment, the present invention provides a novel serine proteinase, referred to herein as "**HELA2**" or "testisin", which has roles in spermatogenesis, in suppressing testicular cancer and as a marker for cancers.

L5 ANSWER 4 OF 6 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 1
ACCESSION NUMBER: 1998-10406 BIOTECHDS
TITLE: New serine proteases and kinase involved in regulating cell activity and viability;
serine protease **HELA2** used to regulate cell activity and viability particularly in the testes, for promotion of sperm production, and diagnosis and suppression of cancer, especially testicular cancer
AUTHOR: Antalis T M; Hooper J D
PATENT ASSIGNEE: Amrad-Oper.
LOCATION: Richmond, Victoria, Australia.
PATENT INFO: WO 9836054 20 Aug 1998
APPLICATION INFO: WO 1998-AU85 13 Feb 1998
PRIORITY INFO: AU 1997-422 18 Nov 1997; AU 1997-5101 13 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-480768 [41]
AB An isolated proteinaceous molecule (A), e.g. **HELA2** (or testin), associated with regulation of cell activity or viability is claimed. (A) is a serine protease and can be amplified by the polymerase chain reaction, using the given DNA primers. (A) can also be any protein with at least 50% identity to the given protein sequences, or encoded by a nucleic acid with at least 50% similarity to the given DNA sequences. Alternatively (A) can be a kinase with a given protein and DNA sequence. Also claimed is a method of regulating cell activity or viability by contacting it with (A). The claims also cover a method of modulating mammal fertility by modulating levels of (A), increasing its levels by introduction of recombinant (A) to facilitate sperm maturation and development. Also covered is a composition containing (A), and an antibody, agonist and antagonist (antisense or ribozyme) capable of interacting with (A). The claims extend to a method of diagnosing cancer or a predisposition to cancer by determining the presence of a sequence encoding (A), as **HELA2** is a suppressor of testicular cancer. (167pp)

L5 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 82162946 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6175442
TITLE: Drug-induced biochemical markers of cancer in cervical carcinoma cells.
AUTHOR: Ghosh N K
SOURCE: Clinical biochemistry, (1982 Feb) 15 (1) 28-33.
Journal code: 0133660. ISSN: 0009-9120.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198206
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19990129
Entered Medline: 19820614
AB The elevation in the serum level of CEA in cancer patients undergoing treatment with 5-FU and other antitumor drugs has been reported. In the present study, the ectopic synthesis of multiple carcinoplacental markers has been observed to be induced (10- to 264-fold) simultaneously in the same cervical carcinoma cells (HeLa65, HeLa71 and **HeLa2**.2) by hydroxyurea and sodium butyrate. Among the drug-induced biochemical markers observed in HeLa cells are four sialopeptides. Regan Isoenzyme (Placental Isoenzyme of Alkaline Phosphatase), HCT-Beta, FSH-Beta, HCG-Alpha and also a steroid hormone, Progesterone. The peptide and steroid hormones were quantitated by specific radioimmunoassays (RIA), in cultured cells, media, and homogenates of tumor tissues. The induction of biochemical markers was observed also with lung carcinoma cells. That

multiple polypeptides, or steroids regulated by them, are simultaneously inducible in the same cancer cells, suggest the proximity on the DNA strand of several oncofetal and oncoplacental genes derepressed by antineoplastic drugs. This fundamental study has had important clinical ramifications. The results may be used to recognize the retention by cancer patients of occult malignancy after radiotherapy or surgery. The unsuspected metastasis may be reflected by a transient rise in the serum level of these markers during chemotherapy with anticancer drugs, which specifically inhibit DNA replication without interfering with the transcription of messenger-RNA and subsequent translation of proteins. The drug-induced protein-hormones, observed in this study, are the products of activated trophoblastic/pituitary genes in the nondividing DNA of neoplastic cells.

L5 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 78055825 MEDLINE
DOCUMENT NUMBER: PubMed ID: 73243
TITLE: [Karyological study of the continuous cell lines. Comparative analysis of the Hela and Detroit-6 cell lines]. Kariologicheskoe issledovanie perevivaemykh kletochnykh linii. I. Sravnitel'nyi analiz linii Hela i Detroit-6.
AUTHOR: Mikhailova G R; Rodova M A; Gadashevich V N; Demidova S A; Zhdanov V M
SOURCE: Tsitologiia, (1977 Jul) 19 (7) 786-90.
Journal code: 0417363. ISSN: 0041-3771.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197801
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19970203
Entered Medline: 19780127
AB Comparison of the results of the karyologic analysis of two Hela cell sublines (HeLa1 and **HeLa2**), obtained from different sources, and of Detroit-6 cell line has shown that all the lines contain marker chromosomes characteristic of the HeLa cell line. Detroit-6 cell line marker chromosomes are similar to markers of the HeLa subline (HeLa1). At the same time, part of marker chromosomes in the two sublines of HeLa cell line (HeLa1 and **HeLa2**) are different. These data show that HeLa1 and Detroit-6 cell lines are more similar than two sublines of the same HeLa cell line.

=> d his

(FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
L1 620411 S PROTEINASE? OR PROTEASE?
L2 394137 S SERINE
L3 104666 S L1 AND L2
L4 9 S "HELA2"
L5 6 DUP REM L4 (3 DUPLICATES REMOVED)

=> s l1 and l5
L6 2 L1 AND L5

=> d 1-2 ibib ab

L6 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:42593 BIOSIS
DOCUMENT NUMBER: PREV200300042593

TITLE: DNA molecules encoding human **HELA2** or testisin serine **proteinases**.
AUTHOR(S): Antalis, Toni Marie [Inventor, Reprint Author]; Hooper, John David [Inventor]
CORPORATE SOURCE: Toowong, Australia
ASSIGNEE: Amrad Operations Pty., Ltd., Victoria, Australia
PATENT INFORMATION: US 6479274 20021112
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 12 2002) Vol. 1264, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB The present invention related generally to novel molecules and more particularly novel proteinaceous molecules involved in or associated with regulation of cell activities and/or viability. The present invention is particularly directed to novel serine **proteinases** and a novel kinase and to derivatives, agonists and antagonists thereof. In one embodiment, the present invention provides a novel serine **proteinase**, referred to herein as "**HELA2**" or "testisin", which has roles in spermatogenesis, in suppressing testicular cancer and as a marker for cancers.

L6 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 1998-10406 BIOTECHDS
TITLE: New serine **proteases** and kinase involved in regulating cell activity and viability; serine **protease HELA2** used to regulate cell activity and viability particularly in the testes, for promotion of sperm production, and diagnosis and suppression of cancer, especially testicular cancer
AUTHOR: Antalis T M; Hooper J D
PATENT ASSIGNEE: Amrad-Oper.
LOCATION: Richmond, Victoria, Australia.
PATENT INFO: WO 9836054 20 Aug 1998
APPLICATION INFO: WO 1998-AU85 13 Feb 1998
PRIORITY INFO: AU 1997-422 18 Nov 1997; AU 1997-5101 13 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-480768 [41]

AB An isolated proteinaceous molecule (A), e.g. **HELA2** (or testin), associated with regulation of cell activity or viability is claimed. (A) is a serine **protease** and can be amplified by the polymerase chain reaction, using the given DNA primers. (A) can also be any protein with at least 50% identity to the given protein sequences, or encoded by a nucleic acid with at least 50% similarity to the given DNA sequences. Alternatively (A) can be a kinase with a given protein and DNA sequence. Also claimed is a method of regulating cell activity or viability by contacting it with (A). The claims also cover a method of modulating mammal fertility by modulating levels of (A), increasing its levels by introduction of recombinant (A) to facilitate sperm maturation and development. Also covered is a composition containing (A), and an antibody, agonist and antagonist (antisense or ribozyme) capable of interacting with (A). The claims extend to a method of diagnosing cancer or a predisposition to cancer by determining the presence of a sequence encoding (A), as **HELA2** is a suppressor of testicular cancer. (167pp)

=> d his

(FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
L1        620411 S PROTEINASE? OR PROTEASE?
L2        394137 S SERINE
L3        104666 S L1 AND L2
L4             9 S "HELA2"
L5             6 DUP REM L4 (3 DUPLICATES REMOVED)
L6             2 S L1 AND L5

=> s testisin
L7            89 TESTISIN

=> s l3 and l7
L8            80 L3 AND L7

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            27 DUP REM L8 (53 DUPLICATES REMOVED)

=> d 1-27 ibib ab

L9   ANSWER 1 OF 27     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2005504685     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 16176265
TITLE:              A novel serine protease highly
                    expressed in the pancreas is expressed in various kinds of
                    cancer cells.
AUTHOR:             Mitsui Shinichi; Okui Akira; Kominami Katsuya; Konishi
                    Eiichi; Uemura Hidetoshi; Yamaguchi Nozomi
CORPORATE SOURCE:   Department of Cell Biology, Research Institute for
                    Geriatrics, Kyoto Prefectural University of Medicine,
                    Japan.
SOURCE:             FEBS J, (2005 Oct) 272 (19) 4911-23.
                    Journal code: 101229646. ISSN: 1742-464X.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200511
ENTRY DATE:         Entered STN: 20050923
                    Last Updated on STN: 20051115
                    Entered Medline: 20051114
AB   We have isolated a cDNA that encodes a novel serine
     protease, prosemin, from human brain.  The cDNA of human prosemin
     is 1306 bp, encoding 317 amino acids.  It showed significant homology with
     the sequence of a chromosome 16 cosmid clone (accession number  NT_037887.4).
     The prosemin gene contains six exons and five introns.  The amino acid
     sequence of prosemin shows significant homology to prostasin,
     gamma-tryptase, and testisin (43%, 41%, and 38% identity,
     respectively), the genes of which are also located on chromosome 16.
     Northern hybridization showed that prosemin is expressed predominantly in
     the pancreas and weakly in the prostate and cerebellum.  However, western
     blot and RT-PCR analyses showed that prosemin is expressed and secreted
     from various kinds of cancer cells, such as glioma, pancreas, prostate,
     and ovarian cell lines.  Prosemin is secreted in the cystic fluid of
     clinical ovarian cancers.  Furthermore, immunohistochemistry showed
     prosemin protein localized in the apical parts of ovarian carcinomas.
     Recombinant prosemin was expressed in COS cells and was purified by
     immunoaffinity chromatography.  Recombinant prosemin preferentially
     cleaved benzyloxycarbonyl (Z)-His-Glu-Lys-methylcoumaryl amidide (MCA) and
     t-butyloxycarbonyl (Boc)-Gln-Ala-Arg-MCA.  Our results suggest that
     prosemin is a novel serine protease of the chromosome
     16 cluster that is highly expressed in the pancreas.  The usefulness of
```

this **serine protease** as a candidate tumor marker should be further examined.

L9 ANSWER 2 OF 27 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005076305 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15705885
TITLE: **Testisin**, a glycosyl-phosphatidylinositol-linked **serine protease**, promotes malignant transformation in vitro and in vivo.
AUTHOR: Tang Tenny; Kmet Muriel; Corral Laura; Vartanian Steffan; Tobler Andreas; Papkoff Jackie
CORPORATE SOURCE: diaDexus Inc., 343 Oyster Point Boulevard, South San Francisco, CA 94080, USA.. jpapkoff@diadexus.com
SOURCE: Cancer research, (2005 Feb 1) 65 (3) 868-78. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050212
Last Updated on STN: 20050315
Entered Medline: 20050314

AB Human **testisin**, a **serine protease**, is highly expressed in ovarian cancer and premeiotic spermatocytes with relatively little expression in other normal tissues. We first showed that **testisin** was localized on the surface of cultured tumor cells as a glycosyl-phosphatidylinositol-linked protein. We next explored the biological function of **testisin** in malignant transformation through manipulation of **testisin** expression in cell culture model systems. Small interfering RNA-mediated knockdown of endogenous **testisin** mRNA and protein expression in tumor cell lines led to increased apoptosis and diminished growth in soft agar. Conversely, overexpression of **testisin** in an epithelial cell line induced colony formation in soft agar as well as s.c. tumor growth in severe combined immunodeficient mice. A catalytic domain mutant was unable to induce soft-agar growth indicating that **testisin protease** activity is required for transformation. Ectopic expression of **testisin** in a human ovarian cancer cell line without endogenous **testisin** expression, led to the formation of larger tumors in severe combined immunodeficient mice. Data presented here provide the first demonstration that **testisin** can promote cellular processes that drive malignant transformation. Our functional data coupled with the restricted normal tissue distribution of **testisin** and its overexpression in a majority of ovarian cancers validates this cell surface protein as a target for therapeutic intervention.

L9 ANSWER 3 OF 27 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005095048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15685234
TITLE: Hypermethylation of the 5' CpG island of the gene encoding the **serine protease Testisin** promotes its loss in testicular tumorigenesis.
AUTHOR: Manton K J; Douglas M L; Netzel-Arnett S; Fitzpatrick D R; Nicol D L; Boyd A W; Clements J A; Antalis T M
CORPORATE SOURCE: Leukaemia Foundation and Cellular Oncology Laboratories, Queensland Institute of Medical Research, Queensland, Australia.
SOURCE: British journal of cancer, (2005 Feb 28) 92 (4) 760-9. Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050224
Last Updated on STN: 20050325
Entered Medline: 20050324

AB The **Testisin** gene (PRSS21) encodes a glycosylphosphatidylinositol (GPI)-linked **serine protease** that exhibits testis tissue-specific expression. Loss of **Testisin** has been implicated in testicular tumorigenesis, but its role in testis biology and tumorigenesis is not known. Here we have investigated the role of CpG methylation in **Testisin** gene inactivation and tested the hypothesis that **Testisin** may act as a tumour suppressor for testicular tumorigenesis. Using sequence analysis of bisulphite-treated genomic DNA, we find a strong relationship between hypermethylation of a 385 bp 5' CpG rich island of the **Testisin** gene, and silencing of the **Testisin** gene in a range of human tumour cell lines and in 100% (eight/eight) of testicular germ cell tumours. We show that treatment of **Testisin**-negative cell lines with demethylating agents and/or a histone deacetylase inhibitor results in reactivation of **Testisin** gene expression, implicating hypermethylation in **Testisin** gene silencing. Stable expression of **Testisin** in the **Testisin**-negative Tera-2 testicular cancer line suppressed tumorigenicity as revealed by inhibition of both anchorage-dependent cell growth and tumour formation in an SCID mouse model of testicular tumorigenesis. Together, these data show that loss of **Testisin** is caused, at least in part, by DNA hypermethylation and histone deacetylation, and suggest a tumour suppressor role for **Testisin** in testicular tumorigenesis.

L9 ANSWER 4 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 2005:372745 BIOSIS
DOCUMENT NUMBER: PREV200510171688
TITLE: On the biological function of **testisin**: a GPI-anchored **serine protease**.
AUTHOR(S): Netzel-Arnett, S. [Reprint Author]; Bugge, T. H.; Hess, R. A.; Antalis, T. M.
CORPORATE SOURCE: Univ Maryland, Sch Med, Dept Physiol and Surg, Rockville, MD USA
SOURCE: Thrombosis and Haemostasis, (APR 2005) Vol. 93, No. 4, pp. A5.
Meeting Info.: 10th Interenational Workshop on Molecular and Cellular Biology of Plasminogen Activation. Washington, DC, USA. April 09 -13, 2005.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Sep 2005
Last Updated on STN: 21 Sep 2005

L9 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:355085 HCAPLUS
DOCUMENT NUMBER: 140:369944
TITLE: Human tissue-specific housekeeping genes identified by expression profiling
INVENTOR(S): Aburatani, Hiroyuki; Yamamoto, Shogo
PATENT ASSIGNEE(S): NGK Insulators, Ltd., Japan
SOURCE: PCT Int. Appl., 372 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035785	A1	20040429	WO 2002-JP10753	20021016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004229233	A1	20041118	US 2003-684422	20031015
PRIORITY APPLN. INFO.:			US 2002-418614P	P 20021016
			WO 2002-JP10753	W 20021016

AB Housekeeping genes commonly expressed in 35 different human tissues, oligonucleotide probes and DNA microarrays containing them, are disclosed.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:142430 HCAPLUS

DOCUMENT NUMBER: 143:23849

TITLE: Development of the new diagnostic and prognostic biomarker of ovarian cancer

AUTHOR(S): Shigemasa, Kazushi

CORPORATE SOURCE: Department of Obstetrics and Gynecology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan

SOURCE: Nippon Sanka Fujinka Gakkai Zasshi (2004), 56(11), 1264-1274
CODEN: NISFAY; ISSN: 0300-9165

PUBLISHER: Nippon Sanka Fujinka Gakkai

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB To develop the new diagnostic and prognostic biomarker of ovarian cancer, we worked on the detection of new **serine proteases** as potential biomarker of ovarian cancer. We also worked on the mol. cloning of CA125 gene to develop the new CA125 assay system based on the CA125 gene structure. CA125 protein is composed of a short C-terminal domain, an extracellular superstructure dominated by repeat sequence, and a glycosylated N-terminal domain. Extracellular superstructure dominated by a repeat domain composed of 156 amino acid repeat units encompass the CA125 antibody (OC125 and M11) epitope binding sites. We developed the real-time PCR assay system targeting N-terminal domain to quantify CA125 mRNA expression and the assay system was compared to the similar assay system targeting the repeat units of CA125. Interestingly, the assay system targeting N-terminal domain showed the better sensitivity to detect early stage ovarian cancer compared to the assay system targeting CA125 repeat units. These results suggest that to develop new CA125 assay system using the new monoclonal antibody to determine CA125 N-terminal domain may be useful as a diagnostic tool for early stage ovarian cancer. To assess the value of secreted **proteases** as markers for early tumor detection and as targets for prognostic biomarker for ovarian cancer, we developed a strategy to detect **serine protease** genes differentially expressed in ovarian cancer using redundant primers to the amino acid sequences comprising the conserved catalytic triad domain of the **serine protease** family (viz. His-Asp-Ser). Using this approach, we have identified membrane type **serine proteases** including hepsin, TADG-12, TADG-15, and **testisin**. We also have identified secretory type **serine proteases** including **protease** M (KLK6), stratum corneum

chymotryptic enzyme (SCCE/KLK7), and TADG-14 (KLK8). These **serine proteases** are abundantly expressed in ovarian cancers compared to normal ovaries. Immunohistochem. showed that these **serine proteases** are expressed in ovarian cancer cells not in underlying stromal cells. The mRNA expression levels of these **serine proteases** including TADG-12, **testisin**, KLK5, and KLK7 are related with advanced clin. stage in ovarian cancer. The survival anal. showed that TADG-12, KLK5, KLK11, and KLK14 are related with poor prognosis in patients with ovarian cancer. These results suggest that the **serine proteases** identified here may play a role in development and progression of ovarian cancer and that some of these **proteases** may be useful as prognostic biomarker of ovarian cancer.

L9 ANSWER 7 OF 27 EMBASE

ACCESSION NUMBER: 2004090618 EMBASE
TITLE: Immunological treatment of ovarian cancer.
AUTHOR: Cannon M.J.; Santin A.D.; O'Brien T.J.
CORPORATE SOURCE: M.J. Cannon, Dept. of Microbiology and Immunology, Univ. of AR for Medical Sciences, 4301 West Markham, Little Rock, AR 72205, United States. mcannon@uams.edu
SOURCE: Current Opinion in Obstetrics and Gynecology, (2004) Vol. 16, No. 1, pp. 87-92.
Refs: 32
ISSN: 1040-872X CODEN: COOGEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040325
Last Updated on STN: 20040325

AB Purpose of review: Development of immunological treatments for ovarian cancer has not been a conspicuous success story over the past few years. Only a handful of clinical trials have reported immunological responses, and correlation with clinical benefit has been elusive. Several recent studies presented in this review, however, point to a revival of optimism for the development of novel immunotherapeutic strategies. Recent findings: The cloning and sequencing of CA125, coupled with novel structural and functional insights, undoubtedly represent important steps forward. The possibility that CA125 could play a role in evasion of immunity by ovarian tumors may represent a new challenge, but does not detract from its potential as a therapeutic target. Of the recent clinical trial reports, the most intriguing results were seen from immunotherapy with a conventional mouse monoclonal antibody specific for CA125, in which human anti-mouse antibody responses correlated significantly with improved survival of patients with advanced stage ovarian cancer and clinical evidence of recurrent disease at the time of treatment. Summary: There is little doubt that CA125 will undergo a renaissance as an important target antigen for development of novel immunological treatments, particularly with regard to cellular therapies. Identification of other novel ovarian tumor antigens will also accelerate research focused on stimulation of T-cell immunity. Current research trends suggest a paradigm shift in emphasis from vaccines designed to elicit antibody responses to strategies such as dendritic cell vaccination that are designed to induce broader immunity, including ovarian tumor antigen-specific helper T-lymphocyte and cytotoxic T-lymphocyte responses.

L9 ANSWER 8 OF 27 BIOSIS
DUPLICATE 5
ACCESSION NUMBER: 2004:438005 BIOSIS

DOCUMENT NUMBER: PREV200400438138
TITLE: On the biological function of **testisin**: A membrane **serine protease** expressed specifically during spermatogenesis.
AUTHOR(S): Netzel-Arnett, S.; Haudenschild, C. C.; Bugge, T. H.; Antalis, T. M.
SOURCE: Journal of Andrology, (March 2004) No. Suppl. S, pp. 55. print.
Meeting Info.: 29th Annual Meeting of the American Society of Andrology. Baltimore, MD, USA. April 17-20, 2004. American Society of Andrology.
ISSN: 0196-3635 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004

L9 ANSWER 9 OF 27 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003042790 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12441343
TITLE: Structure and activity of human pancreasin, a novel tryptic **serine** peptidase expressed primarily by the pancreas.
AUTHOR: Bhagwandin Vikash J; Hau Leola W-T; Mallen-St Clair Jon; Wolters Paul J; Caughey George H
CORPORATE SOURCE: Cardiovascular Research Institute and Department of Medicine, University of California at San Francisco, California 94143-0911, USA.
CONTRACT NUMBER: HL-24136 (NHLBI)
SOURCE: Journal of biological chemistry, (2003 Jan 31) 278 (5) 3363-71. Electronic Publication: 2002-11-18.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY030095
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030129
Last Updated on STN: 20030404
Entered Medline: 20030403

AB In a search for genes encoding the **serine** peptidases prostasin and **testisin**, which are expressed mainly in prostate and testis, respectively, we identified a related, novel gene. Sequencing of cDNA allowed us to deduce the full amino acid sequence of the human gene product, which we term "pancreasin" because it is transcribed strongly in the pancreas. The idiosyncratic 6-exon organization of the gene is shared by a small group of tryptic **proteases**, including prostasin, **testisin**, and gamma-tryptase. Like the other genes, the pancreasin gene resides on chromosome 16p. Pancreasin cDNA predicts a 290-residue, N-glycosylated, **serine** peptidase with a typical signal peptide, a 12-residue activation peptide cleaved by tryptic hydrolysis, and a 256-amino acid catalytic domain. Unlike prostasin and other close relatives, human pancreasin and a nearly identical chimpanzee homologue lack a carboxyl-terminal membrane anchor, although this is present in 328-residue mouse pancreasin, the cDNA of which we also cloned and sequenced. In marked contrast to prostasin, which is 43% identical in the catalytic domain, human pancreasin is transcribed strongly in pancreas (and in the pancreatic ductal adenocarcinoma line, HPAC) but weakly or not at all in kidney and prostate. Antibodies raised against pancreasin detect cytoplasmic expression in HPAC cells. Recombinant, epitope-tagged pancreasin expressed in Chinese hamster ovary cells is glycosylated and secreted as an active tryptic peptidase. Pancreasin's preferences for

hydrolysis of extended peptide substrates feature a strong preference for P1 Arg and differ from those of trypsin. Pancreasin is inhibited by benzamidine and leupeptin but resists several classic inhibitors of trypsin. Thus, pancreasin is a secreted, tryptic **serine protease** of the pancreas with novel physical and enzymatic properties. These studies provide a rationale for exploring the natural targets and roles of this enzyme.

L9 ANSWER 10 OF 27 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003111572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12624642
TITLE: Endothelial cell **serine proteases** expressed during vascular morphogenesis and angiogenesis.
AUTHOR: Aimes Ronald T; Zijlstra Andries; Hooper John D; Ogbourne Steven M; Sit Mae-Le; Fuchs Simone; Gotley David C; Quigley James P; Antalis Toni M
CORPORATE SOURCE: Department of Cell Biology, The Scripps Research Institute, La Jolla, California, USA.
CONTRACT NUMBER: P01 HL31950 (NHLBI)
R01 CA65660 (NCI)
T32 HL07695 (NHLBI)
SOURCE: Thrombosis and haemostasis, (2003 Mar) 89 (3) 561-72. Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030308
Last Updated on STN: 20031031
Entered Medline: 20031030

AB Many **serine proteases** play important regulatory roles in complex biological systems, but only a few have been linked directly with capillary morphogenesis and angiogenesis. Here we provide evidence that **serine protease** activities, independent of the plasminogen activation cascade, are required for microvascular endothelial cell reorganization and capillary morphogenesis in vitro. A homology cloning approach targeting conserved motifs present in all **serine proteases**, was used to identify candidate **serine proteases** involved in these processes, and revealed 5 genes (acrosin, **testisin**, neurosin, PSP and neurotrypsin), none of which had been associated previously with expression in endothelial cells. A subsequent gene-specific RT-PCR screen for 22 **serine proteases** confirmed expression of these 5 genes and identified 7 additional **serine protease** genes expressed by human endothelial cells, urokinase-type plasminogen activator, protein C, TMPRSS2, hepsin, matriptase/MT-SP1, dipeptidylpeptidase IV, and seprase. Differences in **serine protease** gene expression between microvascular and human umbilical vein endothelial cells (HUVECs) were identified and several **serine protease** genes were found to be regulated by the nature of the substratum, ie. artificial basement membrane or fibrillar type I collagen. mRNA transcripts of several **serine protease** genes were associated with blood vessels in vivo by in situ hybridization of human tissue specimens. These data suggest a potential role for **serine proteases**, not previously associated with endothelium, in vascular function and angiogenesis.

L9 ANSWER 11 OF 27 EMBASE
ACCESSION NUMBER: 2003193798 EMBASE
TITLE: Membrane anchored **serine proteases**: A rapidly expanding group of cell surface proteolytic enzymes with potential roles in cancer.

AUTHOR: Netzel-Arnett S.; Hooper J.D.; Szabo R.; Madison E.L.; Quigley J.P.; Bugge T.H.; Antalis T.M.
CORPORATE SOURCE: United States. antalist@usa.redcross.org
SOURCE: Cancer and Metastasis Reviews, (2003) Vol. 22, No. 2-3, pp. 237-258.
Refs: 146
ISSN: 0167-7659 CODEN: CMRED4
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030529
Last Updated on STN: 20030529

AB Dysregulated proteolysis is a hallmark of cancer. Malignant cells require a range of proteolytic activities to enable growth, survival, and expansion. **Serine proteases** of the S1 or trypsin-like family have well recognized roles in the maintenance of normal homeostasis as well as in the pathology of diseases such as cancer. Recently a rapidly expanding subgroup of S1 **proteases** has been recognized that are directly anchored to plasma membranes. These membrane anchored **serine proteases** are anchored either via a carboxy-terminal transmembrane domain (Type I), a carboxy terminal hydrophobic region that functions as a signal for membrane attachment via a glycosyl-phosphatidylinositol linkage (GPI-anchored), or via an amino terminal proximal transmembrane domain (Type II or TTSP). The TTSPs also encode multiple domains in their stem regions that may function in regulatory interactions. The **serine protease** catalytic domains of these enzymes show high homology but also possess features indicating unique substrate specificities. It is likely that the membrane anchored **serine proteases** have evolved to perform complex functions in the regulation of cellular signaling events at the plasma membrane and within the extracellular matrix. Disruption or mutation of several of the genes encoding these **proteases** are associated with disease. Many of the membrane anchored **serine proteases** show restricted tissue distribution in normal cells, but their expression is widely dysregulated during tumor growth and progression. Diagnostic or therapeutic targeting of the membrane anchored **serine proteases** has potential as promising new approaches for the treatment of cancer and other diseases.

L9 ANSWER 12 OF 27 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2003116802 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12630572
TITLE: Cloning, expression analysis, and tissue distribution of esp-1/**testisin**, a membrane-type **serine protease** from the rat.
AUTHOR: Nakamura Yasuo; Inoue Masahiro; Okumura Yuushi; Shiota Mayumi; Nishikawa Mai; Arase Seiji; Kido Hiroshi
CORPORATE SOURCE: Department of Dermatology, The University of Tokushima School of Medicine, Tokushima, Japan.
SOURCE: journal of medical investigation : JMI, (2003 Feb) 50 (1-2) 78-86.
Journal code: 9716841. ISSN: 1343-1420.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030313
Last Updated on STN: 20030513
Entered Medline: 20030509

AB Esp-1/**testisin**, a **serine protease** abundantly expressed in human and mouse testis, is presumed to play an important role in the process of spermatogenesis and fertilization. In this study, we cloned an esp-1/**testisin** cDNA from rats, and analyzed its expression and tissue distribution. The isolated cDNA consisted of 1099 nucleotides with a single open reading frame encoding 328 amino acids and an expected molecular mass of 36.6 kDa. The deduced amino acid sequence of rat Esp-1/**Testisin** had 89% and 62% identity with its murine and human counterparts, respectively, and appeared to be a trypsin-type **serine protease** with a hydrophobic region at the C-terminus. By quantitative real-time polymerase chain reaction analysis, rat esp-1/**testisin** mRNA was predominantly expressed in testis, as in human and mouse. However, its immunohistochemical distribution was predominantly in the elongated spermatids at steps 12 to 19, and not in the primary spermatocytes and round spermatids. This different distribution profile suggests that Esp-1/**Testisin** plays a role in species-specific proteolytic events during spermatogenesis and fertilization.

L9 ANSWER 13 OF 27 EMBASE

ACCESSION NUMBER: 2003182824 EMBASE
TITLE: Genomic overview of **serine proteases**.
AUTHOR: Yousef G.M.; Kopolovic A.D.; Elliott M.B.; Diamandis E.P.
CORPORATE SOURCE: E.P. Diamandis, Dept. of Pathol./Laboratory Medicine, Mount Sinai Hospital, Toronto, Ont. M5G 1X5, Canada. ediamandis@mtsinai.on.ca
SOURCE: Biochemical and Biophysical Research Communications, (23 May 2003) Vol. 305, No. 1, pp. 28-36.
Refs: 39
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030522
Last Updated on STN: 20030522

AB **Serine proteases** (SP) are peptidases with a uniquely activated **serine** residue in the substrate-binding pocket. They represent about 0.6% of all proteins in the human genome. SP are involved in many vital functions such as digestion, blood clotting, fibrinolysis, fertilization, and complement activation and are related to many diseases including cancer, arthritis, and emphysema. In this study, we performed a genomic analysis of human **serine proteases** utilizing different databases, primarily that of MEROPS. SP are distributed along all human chromosomes except 18 and Y with the highest density (23 genes) on chromosome 19. They are either randomly located within the genome or occur in clusters. We identified a number of SP clusters, the largest being the kallikrein cluster on chromosome 19q13.4 which is formed of 15 adjacent genes. Other clusters are located on chromosomes 19p13, 16p13, 14q11, 13q35, 11q22, and 7q35. Genes of each cluster tend to be of comparable sizes and to be transcribed in the same direction. The members of some clusters are sometimes functionally related, e.g., the involvement of many kallikreins in endocrine-related malignancies and the hematopoietic cluster on chromosome 14. It is hypothesized that members of some clusters are under common regulatory mechanisms and might be involved in cascade enzymatic pathways. Several functional domains are found in SP, which reflect their functional diversity. Membrane-type SP tend to cluster in 3 chromosomes and have some common structural domains. Several databases are available for screening, structural and functional

analysis of **serine proteases**. With the near completion of the Human Genome Project, research will be more focused on the interactions between SP and their involvement in pathophysiological processes. .COPYRGT. 2003 Elsevier Science (USA). All rights reserved.

L9 ANSWER 14 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:42593 BIOSIS
DOCUMENT NUMBER: PREV200300042593
TITLE: DNA molecules encoding human HELA2 or **testisin** **serine proteinases**.
AUTHOR(S): Antalis, Toni Marie [Inventor, Reprint Author]; Hooper, John David [Inventor]
CORPORATE SOURCE: Toowong, Australia
ASSIGNEE: Amrad Operations Pty., Ltd., Victoria, Australia
PATENT INFORMATION: US 6479274 20021112
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 12 2002) Vol. 1264, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB The present invention related generally to novel molecules and more particularly novel proteinaceous molecules involved in or associated with regulation of cell activities and/or viability. The present invention is particularly directed to novel **serine proteinases** and a novel kinase and to derivatives, agonists and antagonists thereof. In one embodiment, the present invention provides a novel **serine proteinase**, referred to herein as "HELA2" or "**testisin**", which has roles in spermatogenesis, in suppressing testicular cancer and as a marker for cancers.

L9 ANSWER 15 OF 27 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 2002253113 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11861648
TITLE: A mouse **serine protease** TESP5 is selectively included into lipid rafts of sperm membrane presumably as a glycosylphosphatidylinositol-anchored protein.
AUTHOR: Honda Arata; Yamagata Kazuo; Sugiura Shin; Watanabe Katsuto; Baba Tadashi
CORPORATE SOURCE: Institute of Applied Biochemistry, University of Tsukuba, Tsukuba Science City, Ibaraki 305-8572, Japan.
SOURCE: Journal of biological chemistry, (2002 May 10) 277 (19) 16976-84. Electronic Publication: 2002-02-22. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB059414; GENBANK-AB059415
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020507
Last Updated on STN: 20030105
Entered Medline: 20020613

AB We have previously indicated that at least in mouse, sperm **serine protease**(s) other than acrosin probably act on the limited proteolysis of egg zona pellucida to create a penetration pathway for motile sperm, although the participation of acrosin cannot be ruled out completely. A 42-kDa gelatin-hydrolyzing **serine protease** present in mouse sperm is a candidate enzyme involved in the sperm penetration of the zona pellucida. In this study, we have

PCR-amplified an EST clone encoding a testicular **serine protease**, termed TESP5, and then screened a mouse genomic DNA library using the DNA fragment as a probe. The DNA sequence of the isolated genomic clones indicated that the TESP5 gene is identical to the genes coding for testicular **testisin** and eosinophilic esp-1. Immunochemical analysis using affinity-purified anti-TESP5 antibody revealed that 42- and 41-kDa forms of TESP5 with the isoelectric points of 5.0 to 5.5 are localized in the head, cytoplasmic droplet, and midpiece of cauda epididymal sperm probably as a membranous protein. Moreover, these two forms of TESP5 were selectively included into Triton X-100-insoluble microdomains, lipid rafts, of the sperm membranes. These results show the identity between TESP5/**testisin**/esp-1 and the 42-kDa sperm **serine protease**. When HEK293 cells were transformed by an expression plasmid carrying the entire protein-coding region of TESP5, the recombinant protein produced was released from the cell membrane by treatment with Bacillus cereus phosphatidylinositol-specific phospholipase C, indicating that TESP5 is glycosylphosphatidylinositol-anchored on the cell surface. Enzymatic properties of recombinant TESP5 was similar to but distinguished from those of rat acrosin and pancreatic trypsin by the substrate specificity and inhibitory effects of **serine protease** inhibitors.

L9 ANSWER 16 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:396970 BIOSIS
DOCUMENT NUMBER: PREV200200396970
TITLE: Genomic organization, flanking regions and recombinant expression of mouse prostasin (prss8).
AUTHOR(S): Verghese, George M. [Reprint author]; Caughey, George H. [Reprint author]
CORPORATE SOURCE: Department of Medicine, Cardiovascular Research Institute, University of California, San Francisco, 90 Medical Center Way, Box 0911, San Francisco, CA, 94143-0911, USA
SOURCE: FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1194. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2002
Last Updated on STN: 24 Jul 2002

AB Prostasin is a member of a multigene **serine protease** family and is implicated in epithelial ion channel regulation and tumor invasion. Current goals are to define gene structure and regulatory regions of mouse prostasin and to characterize its **protease** activity. Prss8 was cloned from a 129Sv/J mouse genomic BAC library; transcription start sites were identified by RNA-ligase mediated 5' rapid amplification of cDNA ends. Putative 5' regulatory domains were identified by comparison to TRANSFAC4.0. 4.3kb prss8 gene spans 6 exons organized like human prostasin, tryptase-gamma, **testisin** and DISP. Signal tagged sites localize prss8 to chromosome 7 in an area synteneic to human 16p11. Prss8 3' untranslated region (UTR) and flank overlap a putative orthologue of human MOF. Transcription start sites in 2 initiator elements and a variably spliced 5' UTR intron transcribe 5' UTR variants of mature mProstasin mRNA. The TATA-less promoter, like human prostasin, contains GC and CAAT boxes. Recombinant mProstasin was expressed in insect cells for biochemical characterization. These data provide a basis to study regulation and function of prostasin in mouse models.

L9 ANSWER 17 OF 27 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2002292120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12032451
TITLE: Novel immunotherapeutic strategies in gynecologic oncology. Dendritic cell-based immunotherapy for ovarian cancer.
AUTHOR: Santin A D; Bellone S; Underwood L J; O'Brien T J; Ravaggi A; Pecorelli S; Cannon M J
CORPORATE SOURCE: Department of Otolaryngology, University of Arkansas for Medical Sciences, USA.. santinalessandrod@uams.edu
SOURCE: Minerva ginecologica, (2002 Apr) 54 (2) 133-44. Ref: 80
Journal code: 0400731. ISSN: 0026-4784.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020529
Last Updated on STN: 20021002
Entered Medline: 20021001

AB The recognition of tumor antigen loaded dendritic cells as one of the most promising approaches to induce a tumor specific immune response in vivo has recently generated widespread interest in the use of these natural adjuvants for the therapy of human malignancies refractory to standard treatment modalities. However, many cancer patients may not benefit from current strategies of cancer vaccination because an effective tumor antigen associated with their cancer has not yet been identified or because sufficient amounts of tumor tissue cannot be obtained for antigen preparation. The recent identification and cloning of a group of preferentially expressed **serine proteases** as novel ovarian tumor-associated antigens may offer the opportunity to test in a large group of patients the potential of DC-based immunotherapy. In this review, we describe these ovarian tumor antigens and assess the potential for therapeutic DC vaccination for the treatment of chemotherapy-resistant ovarian cancer.

L9 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:168113 HCAPLUS
DOCUMENT NUMBER: 134:217996
TITLE: Expression vector systems for expression and activation of **serine protease** zymogens
INVENTOR(S): Darrow, Andrew; Qi, Jenson; Andrade-Gordon, Patricia
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016289	A2	20010308	WO 2000-US22283	20000814
WO 2001016289	A3	20010907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6420157	B1	20020716	US 1999-386642	19990831
CA 2382961	AA	20010308	CA 2000-2382961	20000814
EP 1214400	A2	20020619	EP 2000-955526	20000814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003508045	T2	20030304	JP 2001-520837	20000814
PRIORITY APPLN. INFO.:			US 1999-386642	A 19990831
			US 1999-303162	A2 19990430
			WO 2000-US22283	W 20000814

AB DNA sequences are provided encoding an expression vector system that will permit, through limited proteolysis, the activation of expressed zymogen precursor of (S1) **serine proteases** in a highly controlled and reproducible fashion. Nucleic acids encoding pre sequences derived of prolactin and trypsinogen, and pro sequences derived from the EK cleavage site of human trypsinogen I or blood-coagulation factor Xa, are provided. The processed expressed protein, once activated, is rendered in a form amenable to measuring the catalytic activity. This catalytic activity of the activated form, is often a more accurate representation of the mature S1 **protease** gene product relative to the unprocessed zymogen precursor. Thus, this series of zymogen activation constructs represents a significant system for the anal. and characterization of **serine protease** gene products. **Proteases** prostasin, O, neuropsin, F, and MH2 are prepared which may be used in pharmaceutical compns., for the identification of physiol. substrates and specific modulators, for laundry detergents, and in skin care products.

L9 ANSWER 19 OF 27 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER:	2002052778 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 11602603
TITLE:	Human tryptase epsilon (PRSS22), a new member of the chromosome 16p13.3 family of human **serine proteases** expressed in airway epithelial cells.
AUTHOR:	Wong G W; Yasuda S; Madhusudhan M S; Li L; Yang Y; Krilis S A; Sali A; Stevens R L
CORPORATE SOURCE:	Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER:	AI-23483 (NIAID)
	GM-54762 (NIGMS)
	HL-36110 (NHLBI)
	HL-63284 (NHLBI)
SOURCE:	Journal of biological chemistry, (2001 Dec 28) 276 (52) 49169-82. Electronic Publication: 2001-10-15. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
OTHER SOURCE:	GENBANK-AF321182
ENTRY MONTH:	200201
ENTRY DATE:	Entered STN: 20020125
	Last Updated on STN: 20030105
	Entered Medline: 20020131

AB Probing of the GenBank expressed sequence tag (EST) data base with varied human tryptase cDNAs identified two truncated ESTs that subsequently were found to encode overlapping portions of a novel human **serine protease** (designated tryptase epsilon or **protease**, **serine** S1 family member 22 (PRSS22)). The tryptase epsilon gene resides on chromosome 16p13.3 within a 2.5-Mb complex of **serine protease** genes. Although at least 7 of the 14 genes in this complex encode enzymatically active **proteases**, only one tryptase epsilon-like gene was identified. The trachea and esophagus were found to contain the highest steady-state levels of the tryptase epsilon transcript in adult humans. Although the tryptase epsilon transcript was scarce in

adult human lung, it was present in abundance in fetal lung. Thus, the tryptase epsilon gene is expressed in the airways in a developmentally regulated manner that is different from that of other human tryptase genes. At the cellular level, tryptase epsilon is a major product of normal pulmonary epithelial cells, as well as varied transformed epithelial cell lines. Enzymatically active tryptase epsilon is also constitutively secreted from these cells. The amino acid sequence of human tryptase epsilon is 38-44% identical to those of human tryptase alpha, tryptase beta I, tryptase beta II, tryptase beta III, transmembrane tryptase/tryptase gamma, marapsin, and Esp-1/**testisin**. Nevertheless, comparative protein structure modeling and functional studies using recombinant material revealed that tryptase epsilon has a substrate preference distinct from that of its other family members. These data indicate that the products of the chromosome 16p13.3 complex of tryptase genes evolved to carry out varied functions in humans.

L9 ANSWER 20 OF 27 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001247166 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11231276
TITLE: Organization and chromosomal localization of the murine **Testisin** gene encoding a **serine protease** temporally expressed during spermatogenesis.
AUTHOR: Scarman A L; Hooper J D; Boucaut K J; Sit M L; Webb G C; Normyle J F; Antalis T M
CORPORATE SOURCE: The Queensland Institute of Medical Research and the Experimental Oncology Program, University of Queensland, Brisbane, Australia.
SOURCE: European journal of biochemistry / FEBS, (2001 Mar) 268 (5) 1250-8.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF304012; GENBANK-AY005145
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The recently characterized human **serine protease**, **Testisin**, is expressed on premeiotic testicular germ cells and is a candidate type II tumor suppressor for testicular cancer. Here we report the cloning, characterization and expression of the gene encoding mouse **Testisin**, Prss21. The murine **Testisin** gene comprises six exons and five introns and spans approximately 5 kb of genomic DNA with an almost identical structure to the human **Testisin** gene, PRSS21. The gene was localized to murine chromosome 17 A3.3-B; a region syntenic with the location of PRSS21 on human chromosome 16p13.3. Northern blot analyses of RNA from a range of adult murine tissues demonstrated a 1.3 kb mRNA transcript present only in testis. The murine **Testisin** cDNA shares 65% identity with human **Testisin** cDNA and encodes a putative pre-pro-protein of 324 amino acids with 80% similarity to human **Testisin**. The predicted amino-acid sequence includes an N-terminal signal sequence of 27 amino acids, a 27 amino-acid pro-region, a 251 amino-acid catalytic domain typical of a **serine protease** with trypsin-like specificity, and a C-terminal hydrophobic extension which is predicted to function as a membrane anchor. Immunostaining for murine **Testisin** in mouse testis demonstrated specific staining in the cytoplasm and on the plasma membrane of round and elongating spermatids. Examination of murine **Testisin** mRNA expression in developing sperm confirmed that the onset of murine **Testisin** mRNA expression occurred at approximately day 18 after birth, corresponding to the appearance of

spermatids in the testis, in contrast to the expression of human **Testisin** in spermatocytes. These data identify the murine ortholog to human **Testisin** and demonstrate that the murine **Testisin** gene is temporally regulated during murine spermatogenesis.

L9 ANSWER 21 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:1194 BIOSIS
DOCUMENT NUMBER: PREV200200001194
TITLE: The **serine protease testisin** functions as a tumor and/or growth suppressor in testicular tumorgenesis.
AUTHOR(S): Boucaut, Kerry Jane [Reprint author]; Douglas, Meaghan L.; Nicol, David L.; Pera, Martin F.; Clements, Judith A.; Antalis, Toni M.
CORPORATE SOURCE: CMB, Queensland University of Technology, Brisbane, QLD, Australia
kerryB@qimr.edu.au
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 712. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2001
Last Updated on STN: 25 Feb 2002

L9 ANSWER 22 OF 27 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 2001121218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11111072
TITLE: Overexpression of **testisin**, a **serine protease** expressed by testicular germ cells, in epithelial ovarian tumor cells.
AUTHOR: Shigemasa K; Underwood L J; Beard J; Tanimoto H; Ohama K; Parmley T H; O'Brien T J
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hiroshima University School of Medicine, Hiroshima, Japan..
kaz@mcai.med.hiroshima-u.ac.jp
SOURCE: Journal of the Society for Gynecologic Investigation, (2000 Nov-Dec) 7 (6) 358-62.
Journal code: 9433806. ISSN: 1071-5576.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB OBJECTIVE: In a continued effort to identify and characterize secreted **proteases** that are overexpressed in ovarian carcinomas, we discovered the **testisin protease** as such a candidate. When this discovery was originally made, no data existed in the literature or in the GenBank database that identified such a gene. Our main objective was to determine whether this gene was overexpressed exclusively in ovarian tumor tissues compared with normal ovary and whether it was expressed in any other normal tissues. METHODS: mRNA was isolated and cDNA was prepared from 34 ovarian tumors (four adenomas, three low malignant potential tumors, and 27 carcinomas) and seven normal ovaries. The **testisin** mRNA expression level relative to internal control,

beta-tubulin, was determined by Northern blot analysis and semiquantitative polymerase chain reaction (PCR). RESULTS: Northern blot hybridization showed that the **testisin** transcript was abundant in ovarian carcinoma but was not detected in normal ovary. On examination of Northern blots from normal fetal and adult tissues, only adult testis showed abundant transcripts of **testisin**. Semiquantitative PCR examination showed that the **testisin** mRNA levels in ovarian tumors of low malignant potential and in ovarian carcinomas were significantly higher than in normal ovaries ($P < .01$). **Testisin** mRNA level in ovarian carcinomas was also significantly higher than in ovarian adenomas ($P < .05$). **Testisin** overexpression rates in advanced stage (stage 2 or 3) diseases were significantly higher than that in early stage diseases (stage 1) in ovarian carcinoma samples ($P < .05$). CONCLUSIONS: The induction of the **testisin** transcript might contribute to the development, progression, and invasive or metastatic capacity of ovarian carcinomas.

L9 ANSWER 23 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:238467 BIOSIS
DOCUMENT NUMBER: PREV200000238467
TITLE: Localization, structure and regulation of the human PRSS14 gene encoding the **serine proteinase testisin**.
AUTHOR(S): Antalis, Toni M. [Reprint author]; Boucaut, Kerry B. [Reprint author]; Normyle, John F. [Reprint author]; Fitzpatrick, Dave R. [Reprint author]; Hooper, John D. [Reprint author]
CORPORATE SOURCE: Queensland Institute of Med Res, Brisbane, QLD, Australia
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 348. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

L9 ANSWER 24 OF 27 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 2000451880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11004480
TITLE: Localization, expression and genomic structure of the gene encoding the human **serine protease testisin**.
AUTHOR: Hooper J D; Bowen N; Marshall H; Cullen L M; Sood R; Daniels R; Stuttgen M A; Normyle J F; Higgs D R; Kastner D L; Ogbourne S M; Pera M F; Jazwinska E C; Antalis T M
CORPORATE SOURCE: Cellular Oncology Laboratory, The Queensland Institue of Medical Research, Brisbane, Queensland 4029, Australia.
SOURCE: Biochimica et biophysica acta, (2000 Jun 21) 1492 (1) 63-71.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF058301
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001031

AB **Testisin** is a recently identified human **serine protease** expressed by premeiotic testicular germ cells and is a candidate tumor suppressor for testicular cancer. Here, we report the characterization of the gene encoding **testisin**, designated PRSS21, and its localization on the short arm of human chromosome 16 (16p13.3) between the microsatellite marker D16S246 and the radiation hybrid breakpoint CY23HA. We have further refined the localization to cosmid 406D6 in this interval and have established that the gene is approximately 4. 5 kb in length, and contains six exons and five intervening introns. The structure of PRSS21 is very similar to the human prostasin gene (PRSS8) which maps nearby on 16p11.2, suggesting that these genes may have evolved through gene duplication. Sequence analysis showed that the two known isoforms of **testisin** are generated by alternative pre-mRNA splicing. A major transcription initiation site was identified 97 nucleotides upstream of the **testisin** translation start and conforms to a consensus initiator element. The region surrounding the transcription initiation site lacks a TATA consensus sequence, but contains a CCAAT sequence and includes a CpG island. The 5'-flanking region contains several consensus response elements including Sp1, AP1 and several testis-specific elements. Analysis of **testisin** gene expression in tumor cell lines shows that **testisin** is not expressed in testicular tumor cells but is aberrantly expressed in some tumor cell lines of non-testis origin. These data provide the basis for identifying potential genetic alterations of PRSS21 that may underlie both testicular abnormalities and tumorigenesis.

L9 ANSWER 25 OF 27 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1999323395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10397266
TITLE: **Testisin**, a new human **serine proteinase** expressed by premeiotic testicular germ cells and lost in testicular germ cell tumors.
AUTHOR: Hooper J D; Nicol D L; Dickinson J L; Eyre H J; Scarman A L; Normyle J F; Stuttgen M A; Douglas M L; Loveland K A; Sutherland G R; Antalis T M
CORPORATE SOURCE: Cellular Oncology Laboratory, University of Queensland Joint Oncology Program and Queensland Institute of Medical Research, Brisbane, Australia.
SOURCE: Cancer research, (1999 Jul 1) 59 (13) 3199-205. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 20000303
Entered Medline: 19990728

AB We have cloned and characterized a cDNA encoding a new human **serine proteinase, testisin**, that is abundantly expressed only in the testis and is lost in testicular tumors. The **testisin** cDNA was identified by homology cloning using degenerate primers directed at conserved sequence motifs within the catalytic regions of **serine proteinases**. It is 1073 nucleotides long, including 942 nucleotides of open reading frame and a 113-nucleotide 3' untranslated sequence. Northern and dot blot analyses of RNA from a range of normal human tissues revealed a 1.4-kb mRNA species that was present only in testis, which was not detected in eight of eight testicular tumors. **Testisin** cDNA is predicted to encode a protein of 314 amino acids, which consists of a 19-amino acid (aa) signal peptide, a 22-aa proregion, and a 273-aa catalytic domain, including a unique 17-aa COOH-terminal hydrophobic extension that is predicted to function as a membrane anchor. The deduced amino acid sequence of **testisin** shows 44% identity to prostasin and contains features

that are typical of **serine proteinases** with trypsin-like substrate specificity. Antipeptide antibodies directed against the **testisin** polypeptide detected an immunoreactive **testisin** protein of Mr 35,000-39,000 in cell lysates from COS-7 cells that were transiently transfected with **testisin** cDNA. Immunostaining of normal testicular tissue showed that **testisin** was expressed in the cytoplasm and on the plasma membrane of premeiotic germ cells. No staining was detected in eight of eight germ cell-derived testicular tumors. In addition, the **testisin** gene was localized by fluorescence in situ hybridization to the short arm of human chromosome 16 (16p13.3), a region that has been associated with allelic imbalance and loss of heterozygosity in sporadic testicular tumors. These findings demonstrate a new cell surface **serine proteinase**, loss of which may have a direct or indirect role in the progression of testicular tumors of germ cell origin.

L9 ANSWER 26 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 16

ACCESSION NUMBER: 1999:405519 BIOSIS
DOCUMENT NUMBER: PREV199900405519
TITLE: **Testisin**, a new human **serine proteinase** expressed by premeiotic testicular germ cells.
AUTHOR(S): Scarman, A. L. [Reprint author]; Hooper, J. D. [Reprint author]; Normyle, J. F. [Reprint author]; Nicol, D.; Antalis, T. M. [Reprint author]
CORPORATE SOURCE: Cellular Oncology Laboratory, Queensland Institute of Medical Research, Brisbane, QLD, Australia
SOURCE: Biology of Reproduction, (1999) Vol. 60, No. SUPPL. 1, pp. 257. print.
Meeting Info.: Thirty-Second Annual Meeting of the Society for the Study of Reproduction. Pullman, Washington, USA. July 31-August 3, 1999. Society for the Study of Reproduction.
CODEN: BIREBV. ISSN: 0006-3363.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1999
Last Updated on STN: 8 Oct 1999

L9 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:568908 HCAPLUS
DOCUMENT NUMBER: 129:198890
TITLE: Cloning of human **serine proteinases** and a kinase involved in spermatogenesis and the suppression of testicular cancer
INVENTOR(S): Antalis, Toni Marie; Hooper, John David
PATENT ASSIGNEE(S): Amrad Operations Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836054	A1	19980820	WO 1998-AU85	19980213

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
            GA, GN, ML, MR, NE, SN, TD, TG
    AU 9859734          A1    19980908    AU 1998-59734          19980213
    US 6479274          B1    20021112    US 1998-23942          19980213
    AU 774591           B2    20040701    AU 2000-72539          20001228
    US 2003092154       A1    20030515    US 2002-40647          20020107
PRIORITY APPLN. INFO.:                    AU 1997-5101        A  19970213
                                          AU 1997-422         A  19971118
                                          AU 1998-59734       A3 19980213
                                          US 1998-23942       A3 19980213
                                          WO 1998-AU85        W  19980213
AB   The present invention relates novel proteinaceous mols. involved in or
     associated with regulation of cell activities and/or viability.  The present
     invention is particularly directed to novel serine
     proteinases and a novel kinase and to derivs., agonists and
     antagonists thereof.  PCR cloning isolated a human cDNA encoding a novel
     serine proteinase, referred to herein as HELA2 or
     testisin, which has roles in spermatogenesis, in suppressing
     testicular cancer, and as a marker for cancers.  Testisin is
     specifically expressed in the normal testis and is associated with sperm
     development; it is associated with tumors in non-testis cell types and
     testisin mRNA and protein expression is absent in testicular germ
     cell tumors.  The testisin gene was mapped to human chromosome
     16p13.3, and is organized into 6 exons and 5 introns.  Two forms of
     testisin are provided, based on alternative splicing.  The
     testisin gene is associated with a gene cluster of homologous genes,
     designated SP001LA, SP002LA, and SP003LA.  An addnl. serine
     proteinase, designated ATC2, and a kinase designated BCON3 were
     are also provided by PCR cloning with the same primers.
REFERENCE COUNT:          7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
L1       620411 S PROTEINASE? OR PROTEASE?
L2       394137 S SERINE
L3       104666 S L1 AND L2
L4            9 S "HELA2"
L5            6 DUP REM L4 (3 DUPLICATES REMOVED)
L6            2 S L1 AND L5
L7           89 S TESTISIN
L8           80 S L3 AND L7
L9           27 DUP REM L8 (53 DUPLICATES REMOVED)

=> s tumor (a) suppresor
L10          80 TUMOR (A) SUPPRESOR
<------User Break------>


=>
=> s tumor (a) suppressor
L11      149241 TUMOR (A) SUPPRESSOR

=> s l3 and l11
L12         609 L3 AND L11

=> s l7 and l12
L13          15 L7 AND L12
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=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 6 DUP REM L13 (9 DUPLICATES REMOVED)

=> d 1-6 ibib ab

L14 ANSWER 1 OF 6 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 1
ACCESSION NUMBER: 2005150054 EMBASE
TITLE: Hypermethylation of the 5' CpG island of the gene encoding the **serine protease Testisin** promotes its loss in testicular tumorigenesis.
AUTHOR: Manton K.J.; Douglas M.L.; Netzel-Arnett S.; Fitzpatrick D.R.; Nicol D.L.; Boyd A.W.; Clements J.A.; Antalis T.M.
CORPORATE SOURCE: Dr. T.M. Antalis, Department of Physiology, Univ. of Maryland School of Medicine, 15601 Crabbs Branch Way, Rockville, MD 20855, Australia. tantalis@som.umaryland.edu
SOURCE: British Journal of Cancer, (28 Feb 2005) Vol. 92, No. 4, pp. 760-769.
Refs: 62
ISSN: 0007-0920 CODEN: BJCAAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050428
Last Updated on STN: 20050428
AB The **Testisin** gene (PRSS21) encodes a glycosylphosphatidylinositol (GPI)-linked **serine protease** that exhibits testis tissue-specific expression. Loss of **Testisin** has been implicated in testicular tumorigenesis, but its role in testis biology and tumorigenesis is not known. Here we have investigated the role of CpG methylation in **Testisin** gene inactivation and tested the hypothesis that **Testisin** may act as a tumour suppressor for testicular tumorigenesis. Using sequence analysis of bisulphite-treated genomic DNA, we find a strong relationship between hypermethylation of a 385 bp 5' CpG rich island of the **Testisin** gene, and silencing of the **Testisin** gene in a range of human tumour cell lines and in 100% (eight/eight) of testicular germ cell tumours. We show that treatment of **Testisin**-negative cell lines with demethylating agents and/or a histone deacetylase inhibitor results in reactivation of **Testisin** gene expression, implicating hypermethylation in **Testisin** gene silencing. Stable expression of **Testisin** in the **Testisin**-negative Tera-2 testicular cancer line suppressed tumorigenicity as revealed by inhibition of both anchorage-dependent cell growth and tumour formation in an SCID mouse model of testicular tumorigenesis. Together these data show that loss of **Testisin** is caused, at least in part, by DNA hypermethylation and histone deacetylation, and suggest a tumour suppressor role for **Testisin** in testicular tumorigenesis. .COPYRGT. 2005 Cancer Research UK.

L14 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001247166 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11231276
TITLE: Organization and chromosomal localization of the murine **Testisin** gene encoding a **serine protease** temporally expressed during spermatogenesis.
AUTHOR: Scarman A L; Hooper J D; Boucaut K J; Sit M L; Webb G C;

Normyle J F; Antalis T M
CORPORATE SOURCE: The Queensland Institute of Medical Research and the Experimental Oncology Program, University of Queensland, Brisbane, Australia.
SOURCE: European journal of biochemistry / FEBS, (2001 Mar) 268 (5) 1250-8.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF304012; GENBANK-AY005145
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The recently characterized human **serine protease**, **Testisin**, is expressed on premeiotic testicular germ cells and is a candidate type II **tumor suppressor** for testicular cancer. Here we report the cloning, characterization and expression of the gene encoding mouse **Testisin**, Prss21. The murine **Testisin** gene comprises six exons and five introns and spans approximately 5 kb of genomic DNA with an almost identical structure to the human **Testisin** gene, PRSS21. The gene was localized to murine chromosome 17 A3.3-B; a region syntenic with the location of PRSS21 on human chromosome 16p13.3. Northern blot analyses of RNA from a range of adult murine tissues demonstrated a 1.3 kb mRNA transcript present only in testis. The murine **Testisin** cDNA shares 65% identity with human **Testisin** cDNA and encodes a putative pre-pro-protein of 324 amino acids with 80% similarity to human **Testisin**. The predicted amino-acid sequence includes an N-terminal signal sequence of 27 amino acids, a 27 amino-acid pro-region, a 251 amino-acid catalytic domain typical of a **serine protease** with trypsin-like specificity, and a C-terminal hydrophobic extension which is predicted to function as a membrane anchor. Immunostaining for murine **Testisin** in mouse testis demonstrated specific staining in the cytoplasm and on the plasma membrane of round and elongating spermatids. Examination of murine **Testisin** mRNA expression in developing sperm confirmed that the onset of murine **Testisin** mRNA expression occurred at approximately day 18 after birth, corresponding to the appearance of spermatids in the testis, in contrast to the expression of human **Testisin** in spermatocytes. These data identify the murine ortholog to human **Testisin** and demonstrate that the murine **Testisin** gene is temporally regulated during murine spermatogenesis.

L14 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:1194 BIOSIS
DOCUMENT NUMBER: PREV200200001194
TITLE: The **serine protease testisin** functions as a tumor and/or growth suppressor in testicular tumorgenesis.
AUTHOR(S): Boucaut, Kerry Jane [Reprint author]; Douglas, Meaghan L.; Nicol, David L.; Pera, Martin F.; Clements, Judith A.; Antalis, Toni M.
CORPORATE SOURCE: CMB, Queensland University of Technology, Brisbane, QLD, Australia
kerryB@qimr.edu.au
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 712. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2001
Last Updated on STN: 25 Feb 2002

L14 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2000451880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11004480
TITLE: Localization, expression and genomic structure of the gene encoding the human **serine protease testisin**.
AUTHOR: Hooper J D; Bowen N; Marshall H; Cullen L M; Sood R; Daniels R; Stuttgen M A; Normyle J F; Higgs D R; Kastner D L; Ogbourne S M; Pera M F; Jazwinska E C; Antalis T M
CORPORATE SOURCE: Cellular Oncology Laboratory, The Queensland Institue of Medical Research, Brisbane, Queensland 4029, Australia.
SOURCE: Biochimica et biophysica acta, (2000 Jun 21) 1492 (1) 63-71.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF058301
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001031

AB **Testisin** is a recently identified human **serine protease** expressed by premeiotic testicular germ cells and is a candidate **tumor suppressor** for testicular cancer. Here, we report the characterization of the gene encoding **testisin**, designated PRSS21, and its localization on the short arm of human chromosome 16 (16p13.3) between the microsatellite marker D16S246 and the radiation hybrid breakpoint CY23HA. We have further refined the localization to cosmid 406D6 in this interval and have established that the gene is approximately 4. 5 kb in length, and contains six exons and five intervening introns. The structure of PRSS21 is very similar to the human prostasin gene (PRSS8) which maps nearby on 16p11.2, suggesting that these genes may have evolved through gene duplication. Sequence analysis showed that the two known isoforms of **testisin** are generated by alternative pre-mRNA splicing. A major transcription initiation site was identified 97 nucleotides upstream of the **testisin** translation start and conforms to a consensus initiator element. The region surrounding the transcription initiation site lacks a TATA consensus sequence, but contains a CCAAT sequence and includes a CpG island. The 5'-flanking region contains several consensus response elements including Sp1, AP1 and several testis-specific elements. Analysis of **testisin** gene expression in tumor cell lines shows that **testisin** is not expressed in testicular tumor cells but is aberrantly expressed in some tumor cell lines of non-testis origin. These data provide the basis for identifying potential genetic alterations of PRSS21 that may underlie both testicular abnormalities and tumorigenesis.

L14 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:444980 HCAPLUS
DOCUMENT NUMBER: 131:197773
TITLE: **Testisin**, a new human **serine proteinase** expressed by premeiotic testicular germ cells and lost in testicular germ cell tumors
AUTHOR(S): Hooper, John D.; Nicol, David L.; Dickinson, Joanne L.; Eyre, Helen J.; Scarman, Anthony L.; Normyle, John F.; Stuttgen, Melanie A.; Douglas, Meaghan L.;

Loveland, Kate A. Lakoski; Sutherland, Grant R.; Antalis, Toni M.
CORPORATE SOURCE: Cellular Oncology Laboratory, University of Queensland Joint Oncology Program and Queensland Institute of Medical Research, Brisbane, Queensland, 4029, UK
SOURCE: Cancer Research (1999), 59(13), 3199-3205
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have cloned and characterized a cDNA encoding a new human **serine proteinase, testisin**, that is abundantly expressed only in the testis and is lost in testicular tumors. The **testisin** cDNA was identified by homol. cloning using degenerate primers directed at conserved sequence motifs within the catalytic regions of **serine proteinases**. It is 1073 nucleotides long, including 942 nucleotides of open reading frame and a 113-nucleotide 3' untranslated sequence. Northern and dot blot analyses of RNA from a range of normal human tissues revealed a 1.4-kb mRNA species that was present only in testis, which was not detected in eight of eight testicular tumors. **Testisin** cDNA is predicted to encode a protein of 314 amino acids, which consists of a 19-amino acid (aa) signal peptide, a 22-aa proregion, and a 273-aa catalytic domain, including a unique 17-aa COOH-terminal hydrophobic extension that is predicted to function as a membrane anchor. The deduced amino acid sequence of **testisin** shows 44% identity to prostasin and contains features that are typical of **serine proteinases** with trypsin-like substrate specificity. Antipeptide antibodies directed against the **testisin** polypeptide detected an immunoreactive **testisin** protein of Mr 35,000-39,000 in cell lysates from COS-7 cells that were transiently transfected with **testisin** cDNA. Immunostaining of normal testicular tissue showed that **testisin** was expressed in the cytoplasm and on the plasma membrane of premeiotic germ cells. No staining was detected in eight of eight germ cell-derived testicular tumors. In addition, the **testisin** gene was localized by fluorescence in situ hybridization to the short arm of human chromosome 16 (16p13.3), a region that has been associated with allelic imbalance and loss of heterozygosity in sporadic testicular tumors. These findings demonstrate a new cell surface **serine proteinase**, loss of which may have a direct or indirect role in the progression of testicular tumors of germ cell origin.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:568908 HCAPLUS
DOCUMENT NUMBER: 129:198890
TITLE: Cloning of human **serine proteinases** and a kinase involved in spermatogenesis and the suppression of testicular cancer
INVENTOR(S): Antalis, Toni Marie; Hooper, John David
PATENT ASSIGNEE(S): Amrad Operations Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836054	A1	19980820	WO 1998-AU85	19980213

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,

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            KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
            NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
            UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
            FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
            GA, GN, ML, MR, NE, SN, TD, TG
    AU 9859734          A1    19980908    AU 1998-59734          19980213
    US 6479274          B1    20021112    US 1998-23942          19980213
    AU 774591           B2    20040701    AU 2000-72539          20001228
    US 2003092154       A1    20030515    US 2002-40647          20020107
PRIORITY APPLN. INFO.:                      AU 1997-5101        A  19970213
                                            AU 1997-422         A  19971118
                                            AU 1998-59734       A3 19980213
                                            US 1998-23942       A3 19980213
                                            WO 1998-AU85        W  19980213
AB   The present invention relates novel proteinaceous mols. involved in or
     associated with regulation of cell activities and/or viability.  The present
     invention is particularly directed to novel serine
     proteinases and a novel kinase and to derivs., agonists and
     antagonists thereof.  PCR cloning isolated a human cDNA encoding a novel
     serine proteinase, referred to herein as HELA2 or
     testisin, which has roles in spermatogenesis, in suppressing
     testicular cancer, and as a marker for cancers.  Testisin is
     specifically expressed in the normal testis and is associated with sperm
     development; it is associated with tumors in non-testis cell types and
     testisin mRNA and protein expression is absent in testicular germ
     cell tumors.  The testisin gene was mapped to human chromosome
     16p13.3, and is organized into 6 exons and 5 introns.  Two forms of
     testisin are provided, based on alternative splicing.  The
     testisin gene is associated with a gene cluster of homologous genes,
     designated SP001LA, SP002LA, and SP003LA.  An addnl. serine
     proteinase, designated ATC2, and a kinase designated BCON3 were
     are also provided by PCR cloning with the same primers.
REFERENCE COUNT:          7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> e antalis t m/au
E1            1     ANTALIS PATRICIA LYNN/AU
E2           19     ANTALIS T/AU
E3          202 --> ANTALIS T M/AU
E4            1     ANTALIS T M */AU
E5            9     ANTALIS TONI/AU
E6           94     ANTALIS TONI M/AU
E7            6     ANTALIS TONI MARIE/AU
E8            1     ANTALK ISTVAN/AU
E9            5     ANTALKI T/AU
E10           1     ANTALL GLORIA F/AU
E11          40     ANTALL J/AU
E12           1     ANTALL K L/AU

=> s e3-e7
L15         312 ("ANTALIS T M"/AU OR "ANTALIS T M *"/AU OR "ANTALIS TONI"/AU OR
                "ANTALIS TONI M"/AU OR "ANTALIS TONI MARIE"/AU)

=> e hooper j d/au
E1           16     HOOPER J B/AU
E2           29     HOOPER J C/AU
E3           89 --> HOOPER J D/AU
E4            1     HOOPER J D H/AU
E5          186     HOOPER J E/AU
E6            1     HOOPER J E */AU
E7            1     HOOPER J E N/AU
E8           53     HOOPER J F/AU
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E9            1     HOOPER J F G/AU
E10           3     HOOPER J G/AU
E11           1     HOOPER J G V/AU
E12          20     HOOPER J H/AU

=> s e3-e4
L16          90 ("HOOPER J D"/AU OR "HOOPER J D H"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
L1        620411 S PROTEINASE? OR PROTEASE?
L2        394137 S SERINE
L3        104666 S L1 AND L2
L4             9 S "HELA2"
L5             6 DUP REM L4 (3 DUPLICATES REMOVED)
L6             2 S L1 AND L5
L7            89 S TESTISIN
L8            80 S L3 AND L7
L9            27 DUP REM L8 (53 DUPLICATES REMOVED)
L10           80 S TUMOR (A)SUPPRESOR
L11       149241 S TUMOR (A)SUPPRESSOR
L12          609 S L3 AND L11
L13           15 S L7 AND L12
L14            6 DUP REM L13 (9 DUPLICATES REMOVED)
                 E ANTALIS T M/AU
L15          312 S E3-E7
                 E HOOPER J D/AU
L16           90 S E3-E4

=> s l15 or l16
L17         377 L15 OR L16

=> s l1 and l17
L18         155 L1 AND L17

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19           41 DUP REM L18 (114 DUPLICATES REMOVED)

=> d 1-41 ibib ab

L19  ANSWER 1 OF 41     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:  2005136008     MEDLINE
DOCUMENT NUMBER:   PubMed ID: 15767426
TITLE:             Silencing of integrated human papillomavirus type 18
                   oncogene transcription in cells expressing SerpinB2.
AUTHOR:            Darnell Grant A; Antalis Toni M; Rose Barbara R;
                   Suhrbier Andreas
CORPORATE SOURCE:  Queensland Institute of Medical Research, University of
                   Queensland, Brisbane, Queensland, Australia.
CONTRACT NUMBER:   CA098369 (NCI)
SOURCE:            Journal of virology, (2005 Apr) 79 (7) 4246-56.
                   Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:      United States
DOCUMENT TYPE:     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:          English
FILE SEGMENT:      Priority Journals
ENTRY MONTH:       200504
ENTRY DATE:        Entered STN: 20050316
                   Last Updated on STN: 20050427
```

Entered Medline: 20050426

AB The serine **protease** inhibitor SerpinB2 (PAI-2), a major product of differentiating squamous epithelial cells, has recently been shown to bind and protect the retinoblastoma protein (Rb) from degradation. In human papillomavirus type 18 (HPV-18)-transformed epithelial cells the expression of the E6 and E7 oncoproteins is controlled by the HPV-18 upstream regulatory region (URR). Here we illustrate that PAI-2 expression in the HPV-18-transformed cervical carcinoma line HeLa resulted in the restoration of Rb expression, which led to the functional silencing of transcription from the HPV-18 URR. This caused loss of E7 protein expression and restoration of multiple E6- and E7-targeted host proteins, including p53, c-Myc, and c-Jun. Rb expression emerged as sufficient for the transcriptional repression of the URR, with repression mediated via the C/EBPbeta-YY1 binding site (URR 7709 to 7719). In contrast to HeLa cells, where the C/EBPbeta-YY1 dimer binds this site, in PAI-2- and/or Rb-expressing cells the site was occupied by the dominant-negative C/EBPbeta isoform liver-enriched transcriptional inhibitory protein (LIP). PAI-2 expression thus has a potent suppressive effect on HPV-18 oncogene transcription mediated by Rb and LIP, a finding with potential implications for prognosis and treatment of HPV-transformed lesions.

L19 ANSWER 2 OF 41 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005095048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15685234
TITLE: Hypermethylation of the 5' CpG island of the gene encoding the serine **protease** Testisin promotes its loss in testicular tumorigenesis.
AUTHOR: Manton K J; Douglas M L; Netzel-Arnett S; Fitzpatrick D R; Nicol D L; Boyd A W; Clements J A; **Antalis T M**
CORPORATE SOURCE: Leukaemia Foundation and Cellular Oncology Laboratories, Queensland Institute of Medical Research, Queensland, Australia.
SOURCE: British journal of cancer, (2005 Feb 28) 92 (4) 760-9. Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20050224
Last Updated on STN: 20050325
Entered Medline: 20050324

AB The Testisin gene (PRSS21) encodes a glycosylphosphatidylinositol (GPI)-linked serine **protease** that exhibits testis tissue-specific expression. Loss of Testisin has been implicated in testicular tumorigenesis, but its role in testis biology and tumorigenesis is not known. Here we have investigated the role of CpG methylation in Testisin gene inactivation and tested the hypothesis that Testisin may act as a tumour suppressor for testicular tumorigenesis. Using sequence analysis of bisulphite-treated genomic DNA, we find a strong relationship between hypermethylation of a 385 bp 5' CpG rich island of the Testisin gene, and silencing of the Testisin gene in a range of human tumour cell lines and in 100% (eight/eight) of testicular germ cell tumours. We show that treatment of Testisin-negative cell lines with demethylating agents and/or a histone deacetylase inhibitor results in reactivation of Testisin gene expression, implicating hypermethylation in Testisin gene silencing. Stable expression of Testisin in the Testisin-negative Tera-2 testicular cancer line suppressed tumorigenicity as revealed by inhibition of both anchorage-dependent cell growth and tumour formation in an SCID mouse model of testicular tumorigenesis. Together, these data show that loss of Testisin is caused, at least in part, by DNA hypermethylation and histone deacetylation, and suggest a tumour suppressor role for Testisin in testicular tumorigenesis.

L19 ANSWER 3 OF 41 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005160787 EMBASE
TITLE: Amalfi to Washington D.C. - Twenty years of plasminogen activator research.
AUTHOR: **Antalis T.M.**; Bugge T.H.; Lawrence D.A.; Netzel-Arnett S.; Schwartz B.S.; Strickland D.K.
CORPORATE SOURCE: T.H. Bugge, National Institutes of Health, Oral and Pharyngeal Branch, 30 Convent Drive, Bethesda, MD 20852, United States. thomas.bugge@nih.gov
SOURCE: Thrombosis and Haemostasis, (2005) Vol. 93, No. 4, pp. 625-626.
Refs: 7
ISSN: 0340-6245 CODEN: THHADQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20050428
Last Updated on STN: 20050428

L19 ANSWER 4 OF 41 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005419258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15853774
TITLE: Matriptase-3 is a novel phylogenetically preserved membrane-anchored serine **protease** with broad serpin reactivity.
AUTHOR: Szabo Roman; Netzel-Arnett Sarah; Hobson John P; **Antalis Toni M**; Bugge Thomas H
CORPORATE SOURCE: Proteases and Tissue Remodeling Unit, Oral and Pharyngeal Cancer Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, 30 Convent Drive, Bethesda, MD 20892, USA.
CONTRACT NUMBER: CA098369 (NCI)
SOURCE: Biochemical journal, (2005 Aug 15) 390 (Pt 1) 231-42.
Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 20050809
Last Updated on STN: 20051108
Entered Medline: 20051107

AB We report in the present study the bioinformatic identification, molecular cloning and biological characterization of matriptase-3, a novel membrane-anchored serine **protease** that is phylogenetically preserved in fish, birds, rodents, canines and primates. The gene encoding matriptase-3 is located on syntenic regions of human chromosome 3q13.2, mouse chromosome 16B5, rat chromosome 11q21 and chicken chromosome 1. Bioinformatic analysis combined with cDNA cloning predicts a functional TTSP (type II transmembrane serine **protease**) with 31% amino acid identity with both matriptase/MT-SP1 and matriptase-2. This novel **protease** is composed of a short N-terminal cytoplasmic region followed by a transmembrane domain, a stem region with one SEA, two CUB and three LDLRa (low-density lipoprotein receptor domain class A) domains and a C-terminal catalytic serine **protease** domain. Transcript analysis revealed restricted, species-conserved expression of matriptase-3, with the highest mRNA levels in brain, skin, reproductive

and oropharyngeal tissues. The full-length matriptase-3 cDNA directed the expression of a 90 kDa N-glycosylated protein that localized to the cell surface, as assessed by cell-surface biotin labelling. The purified activated matriptase-3 serine **protease** domain expressed in insect cells hydrolysed synthetic peptide substrates, with a strong preference for Arg at position P(1), and showed proteolytic activity towards several macromolecular substrates, including gelatin, casein and albumin. Interestingly, activated matriptase-3 formed stable inhibitor complexes with an array of serpins, including plasminogen activator inhibitor-1, protein C inhibitor, alpha1-**proteinase** inhibitor, alpha2-antiplasmin and antithrombin III. Our study identifies matriptase-3 as a novel biologically active TTSP of the matriptase subfamily having a unique expression pattern and post-translational regulation.

L19 ANSWER 5 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 2005:372794 BIOSIS
DOCUMENT NUMBER: PREV200510171737
TITLE: Matriptase-3 is a novel, evolutionarily conserved matriptase/MT-SP1 homologue that encodes a functional type II transmembrane serine **protease** with conserved expression in mice and humans.
AUTHOR(S): Szabo, R. [Reprint Author]; Netzel-Arnett, S.; Hobson, J. P.; **Antalis, T. M.**; Bugge, T. H.
CORPORATE SOURCE: Natl Inst Dent and Craniofacial Res, Proteases and Tissue Remodeling Unit, NIH, Bethesda, MD 20892 USA
SOURCE: Thrombosis and Haemostasis, (APR 2005) Vol. 93, No. 4, pp. A17.
Meeting Info.: 10th Interenational Workshop on Molecular and Cellular Biology of Plasminogen Activation. Washington, DC, USA. April 09 -13, 2005.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Sep 2005
Last Updated on STN: 21 Sep 2005

L19 ANSWER 6 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 5
ACCESSION NUMBER: 2005:372790 BIOSIS
DOCUMENT NUMBER: PREV200510171733
TITLE: Functional characterization of DESC3; a novel type II transmembrane serine **protease**.
AUTHOR(S): Wagenaar-Miller, R. A. [Reprint Author]; Netzel-Arnett, S.; Hobson, J. P.; **Antalis, T. M.**; Bugge, T. H.
CORPORATE SOURCE: Natl Inst Dent and Craniofacial Res, Proteases and Tissue Remodeling Unit, NIH, Bethesda, MD 20892 USA
SOURCE: Thrombosis and Haemostasis, (APR 2005) Vol. 93, No. 4, pp. A16.
Meeting Info.: 10th Interenational Workshop on Molecular and Cellular Biology of Plasminogen Activation. Washington, DC, USA. April 09 -13, 2005.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Sep 2005
Last Updated on STN: 21 Sep 2005

L19 ANSWER 7 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 6
ACCESSION NUMBER: 2005:372789 BIOSIS

DOCUMENT NUMBER: PREV200510171732
TITLE: DESC1, a member of a large new subfamily of type II transmembrane serine **proteases**, forms serpin inhibitory complexes.
AUTHOR(S): Hobson, J. P. [Reprint Author]; Netzel-Arnett, S.; Szabo, R.; Rehault, S. M.; Church, F. C.; Strickland, D. K.; Lawrence, D. A.; **Antalis, T. M.**; Bugge, T. H.
CORPORATE SOURCE: Natl Inst Dent and Craniofacial Res, Proteases and Tissue Remodelling Unit, NIH, Bethesda, MD 20892 USA
SOURCE: Thrombosis and Haemostasis, (APR 2005) Vol. 93, No. 4, pp. A16.
Meeting Info.: 10th Interenational Workshop on Molecular and Cellular Biology of Plasminogen Activation. Washington, DC, USA. April 09 -13, 2005.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Sep 2005
Last Updated on STN: 21 Sep 2005

L19 ANSWER 8 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 7
ACCESSION NUMBER: 2005:372745 BIOSIS
DOCUMENT NUMBER: PREV200510171688
TITLE: On the biological function of testisin: a GPI-anchored serine **protease**.
AUTHOR(S): Netzel-Arnett, S. [Reprint Author]; Bugge, T. H.; Hess, R. A.; **Antalis, T. M.**
CORPORATE SOURCE: Univ Maryland, Sch Med, Dept Physiol and Surg, Rockville, MD USA
SOURCE: Thrombosis and Haemostasis, (APR 2005) Vol. 93, No. 4, pp. A5.
Meeting Info.: 10th Interenational Workshop on Molecular and Cellular Biology of Plasminogen Activation. Washington, DC, USA. April 09 -13, 2005.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Sep 2005
Last Updated on STN: 21 Sep 2005

L19 ANSWER 9 OF 41 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2004545201 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15328353
TITLE: Mouse DESC1 is located within a cluster of seven DESC1-like genes and encodes a type II transmembrane serine **protease** that forms serpin inhibitory complexes.
AUTHOR: Hobson John P; Netzel-Arnett Sarah; Szabo Roman; Rehault Sophie M; Church Frank C; Strickland Dudley K; Lawrence Daniel A; **Antalis Toni M**; Bugge Thomas H
CORPORATE SOURCE: Proteases and Tissue Remodeling Unit, NIDCR, National Institutes of Health, Bethesda, Maryland 20892, USA.
CONTRACT NUMBER: CA098369 (NCI)
HL-06350 (NHLBI)
HL007698 (NHLBI)
HL32656 (NHLBI)
HL50710 (NHLBI)
HL50784 (NHLBI)
HL54710 (NHLBI)
HL55374 (NHLBI)
HL55747 (NHLBI)
SOURCE: Journal of biological chemistry, (2004 Nov 5) 279 (45)

46981-94. Electronic Publication: 2004-08-24.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041102
Last Updated on STN: 20041229
Entered Medline: 20041228

AB We report the identification and functional analysis of a type II transmembrane serine **protease** encoded by the mouse differentially expressed in squamous cell carcinoma (DESC) 1 gene, and the definition of a cluster of seven homologous DESC1-like genes within a 0.5-Mb region of mouse chromosome 5E1. This locus is syntenic to a region of human chromosome 4q13.3 containing the human orthologues of four of the mouse DESC1-like genes. Bioinformatic analysis indicated that all seven DESC1-like genes encode functional **proteases**. Direct cDNA cloning showed that mouse DESC1 encodes a multidomain serine **protease** with an N-terminal signal anchor, a SEA (sea urchin sperm protein, enterokinase, and agrin) domain, and a C-terminal serine **protease** domain. The mouse DESC1 mRNA was present in epidermal, oral, and male reproductive tissues and directed the translation of a membrane-associated 60-kDa N-glycosylated protein with type II topology. Mouse DESC1 was synthesized in insect cells as a zymogen that could be activated by exposure to trypsin. The purified activated DESC1 hydrolyzed synthetic peptide substrates, showing a preference for Arg in the P1 position. DESC1 proteolytic activity was abolished by generic inhibitors of serine **proteases** but not by other classes of **protease** inhibitors. Most interestingly, DESC1 formed stable inhibitory complexes with both plasminogen activator inhibitor-1 and protein C inhibitor that are expressed in the same tissues with DESC1, suggesting that type II transmembrane serine **proteases** may be novel targets for serpin inhibition. Together, these data show that mouse DESC1 encodes a functional cell surface serine **protease** that may have important functions in the epidermis, oral, and reproductive epithelium.

L19 ANSWER 10 OF 41 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2004003192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14698625
TITLE: Serpin mutagenesis.
AUTHOR: **Antalis Toni M**; Lawrence Daniel A
CORPORATE SOURCE: Department of Vascular Biology, The Jerome H. Holland Laboratory for the Biomedical Sciences, American Red Cross, Rockville, MD 20855, USA.. antalist@usa.redcross.org
SOURCE: Methods (San Diego, Calif.), (2004 Feb) 32 (2) 130-40.
Journal code: 9426302. ISSN: 1046-2023.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040106
Last Updated on STN: 20040901
Entered Medline: 20040831

AB Mutagenesis represents a powerful methodology for the analysis of protein structural and functional relationships and dissection of complex protein-protein interactions. The suicide substrate-like inhibitory mechanism of the proteins of the serpin superfamily offers unique challenges for the design of mutagenesis studies. All serpins share a well-characterized core structure and most adopt a metastable conformation that is required for inhibitory activity. Mutagenesis studies focused on the reactive center loop, the hinge region, **protease**-binding exo-sites, conformational stability, and accessory ligand binding domains

have led to a well-established serpin inhibitory mechanism and have defined specific biological interactions and functions for a number of serpins in development, homeostasis, and host defense. Nonetheless, great care must be taken in the design and interpretation of serpin mutagenesis studies, since the rapid conformational changes that occur during serpin inhibition can be affected at many levels.

L19 ANSWER 11 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 10

ACCESSION NUMBER: 2004:438005 BIOSIS
DOCUMENT NUMBER: PREV200400438138
TITLE: On the biological function of testisin: A membrane serine **protease** expressed specifically during spermatogenesis.
AUTHOR(S): Netzel-Arnett, S.; Haudenschild, C. C.; Bugge, T. H.; **Antalis, T. M.**
SOURCE: Journal of Andrology, (March 2004) No. Suppl. S, pp. 55. print.
Meeting Info.: 29th Annual Meeting of the American Society of Andrology. Baltimore, MD, USA. April 17-20, 2004. American Society of Andrology.
ISSN: 0196-3635 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004

L19 ANSWER 12 OF 41 MEDLINE on STN DUPLICATE 11

ACCESSION NUMBER: 2003426148 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12944478
TITLE: Inhibition of retinoblastoma protein degradation by interaction with the serpin plasminogen activator inhibitor 2 via a novel consensus motif.
AUTHOR: Darnell Grant A; **Antalis Toni M**; Johnstone Ricky W; Stringer Brett W; Ogbourne Steven M; Harrich David; Suhrbier Andreas
CORPORATE SOURCE: Australian National Centre for International and Tropical Health and Nutrition, Queensland Institute of Medical Research and University of Queensland, 300 Herston Road, Brisbane, Queensland 4029, Australia.
SOURCE: Molecular and cellular biology, (2003 Sep) 23 (18) 6520-32.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030912
Last Updated on STN: 20031024
Entered Medline: 20031023

AB Plasminogen activator inhibitor-2 (PAI-2) is well documented as an inhibitor of the extracellular serine **proteinase** urokinase-type plasminogen activator (uPA) and is expressed in activated monocytes and macrophages, differentiating keratinocytes, and many tumors. Here we show that PAI-2 has a novel intracellular function as a retinoblastoma protein (Rb)-binding protein. PAI-2 colocalized with Rb in the nucleus and inhibited the turnover of Rb, which led to increases in Rb protein levels and Rb-mediated activities. Although PAI-2 contains an LXCXE motif, Rb binding was primarily mediated by the C-D interhelical region of PAI-2, which was found to bind to the C pocket of Rb. The C-D interhelical region of PAI-2 contained a novel Rb-binding motif, termed the PENF homology motif, which is shared by many cellular and viral Rb-binding proteins. PAI-2 expression also protected Rb from the accelerated

degradation mediated by human papillomavirus (HPV) E7, leading to recovery of Rb and inhibition of E6/E7 mRNA expression. Protection of Rb by PAI-2 begins to explain many of the diverse, uPA-independent phenotypes conferred by PAI-2 expression. These results indicate that PAI-2 may enhance Rb's tumor suppressor activity and suggest a potential therapeutic role for PAI-2 against HPV-transformed lesions.

L19 ANSWER 13 OF 41 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:284493 SCISEARCH
THE GENUINE ARTICLE: 657QQ
TITLE: Subtractive immunization using highly metastatic human tumor cells identifies SIMA135/CDCP1, a 135 kDa cell surface phosphorylated glycoprotein antigen
AUTHOR: **Hooper J D**; Zijlstra A; Aimes R T; Liang H Y; Claassen G F; Tarin D; Testa J E; Quigley J P (Reprint)
CORPORATE SOURCE: Scripps Res Inst, Dept Cell Biol, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Res Inst, Dept Cell Biol, La Jolla, CA 92037 USA; Univ Calif San Diego, Dept Pathol, La Jolla, CA 92093 USA
jquigley@scripps.edu
COUNTRY OF AUTHOR: USA
SOURCE: ONCOGENE, (27 MAR 2003) Vol. 22, No. 12, pp. 1783-1794. ISSN: 0950-9232.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 11 Apr 2003
Last Updated on STN: 11 Apr 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have previously used a subtractive immunization (SI) approach to generate monoclonal antibodies (mAbs) against proteins preferentially expressed by the highly metastatic human epidermoid carcinoma cell line, M(+)HEp3. Here we report the immunopurification, identification and characterization of SIMA135/CDCP1 (subtractive immunization M(+)HEp3 associated 135kDa protein/CUB domain containing protein 1) using one of these mAbs designated 41-2. Protein expression levels of SIMA135/CDCP1 correlated with the metastatic ability of variant HEp3 cell lines. Protein sequence analysis predicted a cell surface location and type I orientation of SIMA135/CDCP1, which was confirmed directly by immunocytochemistry. Analysis of deglycosylated cell lysates indicated that up to 40 kDa of the apparent molecular weight of SIMA135/CDCP1 is because of N-glycosylation. Western blot analysis using a antiphosphotyrosine antibody demonstrated that SIMA135/CDCP1 from HEp3 cells is tyrosine phosphorylated. Selective inhibitor studies indicated that an Src kinase family member is involved in the tyrosine phosphorylation of the protein. In addition to high expression in M(+)HEp3 cells, the SIMA135/CDCP1 protein is expressed to varying levels in 13 other human tumor cell lines, manifesting only a weak correlation with the reported metastatic ability of these tumor cell lines. The protein is not detected in normal human fibroblasts and endothelial cells. Northern blot analysis indicated that SIMA135/CDCP1 mRNA has a restricted expression pattern in normal human tissues with highest levels of expression in skeletal muscle and colon. Immunohistochemical analysis indicated apical and basal plasma membrane expression of SIMA135/CDCP1 in epithelial cells in normal colon. in colon tumor, SIMA135/CDCP1 expression appeared dysregulated showing extensive cell surface as well as cytoplasmic expression. Consistent with in vitro shedding experiments on HEp3 cells, SIMA135/CDCP1 was also detected within the lumen of normal and cancerous colon crypts, suggesting that protein shedding may occur in vivo. Thus, specific immunodetection followed by proteomic analysis allows for the identification and partial characterization of a heretofore

uncharacterized human cell surface antigen.

L19 ANSWER 14 OF 41 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 12

ACCESSION NUMBER: 2003329749 EMBASE
TITLE: Mouse matriptase-2: Identification, characterization and comparative mRNA expression analysis with mouse hepsin in adult and embryonic tissues.
AUTHOR: **Hooper J.D.**; Campagnolo L.; Goodarzi G.; Truong T.N.; Stuhlmann H.; Quigley J.P.
CORPORATE SOURCE: J.P. Quigley, Division of Vascular Biology, Department of Cell Biology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037, United States. jquigley@scripps.edu
SOURCE: Biochemical Journal, (1 Aug 2003) Vol. 373, No. 3, pp. 689-702.
Refs: 59
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030904
Last Updated on STN: 20030904

AB We report the identification and characterization of mouse matriptase-2 (m-matriptase-2), an 811-amino-acid protein composed of an N-terminal cytoplasmic domain, a membrane-spanning domain, two CUB (complement protein subcomponents C1r/C1s, urchin embryonic growth factor and bone morphogenetic protein 1) domains, three LDLR (low-density-lipoprotein receptor class A) domains and a C-terminal serine-**protease** domain. All m-matriptase-2 protein domain boundaries corresponded with intron/exon junctions of the encoding gene, which spans approx. 29 kb and comprises 18 exons. Matriptase-2 is highly conserved in human, mouse and rat, with the rat matriptase-2 gene (r-maltriptase-2) predicted to encode transmembrane and soluble isoforms. Western-blot analysis indicated that m-matriptase-2 migrates close to its theoretical molecular mass of 91 kDa, and immunofluorescence analysis was consistent with the proposed surface membrane localization of this protein. Reverse-transcription PCR and in-situ-hybridization analysis indicated that m-matriptase-2 expression overlaps with the distribution of mouse hepsin (m-hepsin, a cell-surface serine **protease** identified in hepatoma cells) in adult tissues and during embryonic development. In adult tissues both are expressed at highest levels in liver, kidney and uterus. During embryogenesis m-matriptase-2 expression peaked between days 12.5 and 15.5. m-hepsin expression was biphasic, with peaks at day 7.5 to 8.5 and again between days 12.5 and 15.5. In situ hybridization of embryonic tissues indicated abundant expression of both m-matriptase-2 and m-hepsin in the developing liver and at lower levels in developing pharyngo-tympanic tubes. While m-hepsin was detected in the residual embryonic yolk sac and with lower intensity in lung, heart, gastrointestinal tract, developing kidney tubules and epithelium of the oral cavity, m-matriptase-2 was absent in these tissues, but strongly expressed within the nasal cavity by olfactory epithelial cells. Mechanistic insight into the potential role of this new transmembrane serine **protease** is provided by its novel expression profile in embryonic and adult mouse.

L19 ANSWER 15 OF 41 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 2003111572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12624642
TITLE: Endothelial cell serine **proteases** expressed during vascular morphogenesis and angiogenesis.
AUTHOR: Aimes Ronald T; Zijlstra Andries; Hooper John D; Ogbourne Steven M; Sit Mae-Le; Fuchs Simone; Gotley David C; Quigley

James P; **Antalis Toni M**
CORPORATE SOURCE: Department of Cell Biology, The Scripps Research Institute, La Jolla, California, USA.
CONTRACT NUMBER: P01 HL31950 (NHLBI)
R01 CA65660 (NCI)
T32 HL07695 (NHLBI)
SOURCE: Thrombosis and haemostasis, (2003 Mar) 89 (3) 561-72.
Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030308
Last Updated on STN: 20031031
Entered Medline: 20031030

AB Many serine **proteases** play important regulatory roles in complex biological systems, but only a few have been linked directly with capillary morphogenesis and angiogenesis. Here we provide evidence that serine **protease** activities, independent of the plasminogen activation cascade, are required for microvascular endothelial cell reorganization and capillary morphogenesis in vitro. A homology cloning approach targeting conserved motifs present in all serine **proteases**, was used to identify candidate serine **proteases** involved in these processes, and revealed 5 genes (acrosin, testisin, neurosin, PSP and neurotrypsin), none of which had been associated previously with expression in endothelial cells. A subsequent gene-specific RT-PCR screen for 22 serine **proteases** confirmed expression of these 5 genes and identified 7 additional serine **protease** genes expressed by human endothelial cells, urokinase-type plasminogen activator, protein C, TMPRSS2, hepsin, matriptase/MT-SP1, dipeptidylpeptidase IV, and seprase. Differences in serine **protease** gene expression between microvascular and human umbilical vein endothelial cells (HUVECs) were identified and several serine **protease** genes were found to be regulated by the nature of the substratum, ie. artificial basement membrane or fibrillar type I collagen. mRNA transcripts of several serine **protease** genes were associated with blood vessels in vivo by in situ hybridization of human tissue specimens. These data suggest a potential role for serine **proteases**, not previously associated with endothelium, in vascular function and angiogenesis.

L19 ANSWER 16 OF 41 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2003259433 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12784999
TITLE: Membrane anchored serine **proteases**: a rapidly expanding group of cell surface proteolytic enzymes with potential roles in cancer.
AUTHOR: Netzel-Arnett Sarah; Hooper John D; Szabo Roman; Madison Edwin L; Quigley James P; Bugge Thomas H; **Antalis Toni M**
CORPORATE SOURCE: Vascular Biology Department, Jerome H. Holland Laboratory for the Biological Sciences, American Red Cross, 15601 Crabbs Branch Way, Rockville, MD 20855, USA.
SOURCE: Cancer and metastasis reviews, (2003 Jun-Sep) 22 (2-3) 237-58. Ref: 146
Journal code: 8605731. ISSN: 0167-7659.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20030606

Last Updated on STN: 20040203
Entered Medline: 20040202

AB Dysregulated proteolysis is a hallmark of cancer. Malignant cells require a range of proteolytic activities to enable growth, survival, and expansion. Serine **proteases** of the S1 or trypsin-like family have well recognized roles in the maintenance of normal homeostasis as well as in the pathology of diseases such as cancer. Recently a rapidly expanding subgroup of S1 **proteases** has been recognized that are directly anchored to plasma membranes. These membrane anchored serine **proteases** are anchored either via a carboxy-terminal transmembrane domain (Type I), a carboxy terminal hydrophobic region that functions as a signal for membrane attachment via a glycosyl-phosphatidylinositol linkage (GPI-anchored), or via an amino terminal proximal transmembrane domain (Type II or TTSP). The TTSPs also encode multiple domains in their stem regions that may function in regulatory interactions. The serine **protease** catalytic domains of these enzymes show high homology but also possess features indicating unique substrate specificities. It is likely that the membrane anchored serine **proteases** have evolved to perform complex functions in the regulation of cellular signaling events at the plasma membrane and within the extracellular matrix. Disruption or mutation of several of the genes encoding these **proteases** are associated with disease. Many of the membrane anchored serine **proteases** show restricted tissue distribution in normal cells, but their expression is widely dysregulated during tumor growth and progression. Diagnostic or therapeutic targeting of the membrane anchored serine **proteases** has potential as promising new approaches for the treatment of cancer and other diseases.

L19 ANSWER 17 OF 41 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2003356156 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12888865
TITLE: Type II transmembrane serine **proteases**.
AUTHOR: Szabo Roman; Wu Qingyu; Dickson Robert B; Netzel-Arnett Sarah; **Antalis Toni M**; Bugge Thomas H
CORPORATE SOURCE: Oral and Pharyngeal Cancer Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Thrombosis and haemostasis, (2003 Aug) 90 (2) 185-93. Ref: 81
Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20030731
Last Updated on STN: 20040512
Entered Medline: 20040511

AB The recent availability of human and mouse genome sequences and expressed sequence tag databases facilitated the identification of a large new family of membrane anchored serine **proteases**, the type II transmembrane serine **proteases** or TTSPs. Analyses of human inherited disorders and gene targeting studies in mice have revealed that several members of this new **protease** family have critical functions in development and health. Preliminary studies also suggest that aberrant expression of type II transmembrane serine **proteases** may be linked to disease progression. The knowledge gathered thus far of the genetics, physiology, and pathology of this interesting new serine **protease** family will be reviewed here in brief.

L19 ANSWER 18 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:42593 BIOSIS
DOCUMENT NUMBER: PREV200300042593
TITLE: DNA molecules encoding human HELA2 or testisin serine **proteinases**.
AUTHOR(S): **Antalis, Toni Marie** [Inventor, Reprint Author]; Hooper, John David [Inventor]
CORPORATE SOURCE: Toowong, Australia
ASSIGNEE: Amrad Operations Pty., Ltd., Victoria, Australia
PATENT INFORMATION: US 6479274 20021112
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 12 2002) Vol. 1264, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB The present invention related generally to novel molecules and more particularly novel proteinaceous molecules involved in or associated with regulation of cell activities and/or viability. The present invention is particularly directed to novel serine **proteinases** and a novel kinase and to derivatives, agonists and antagonists thereof. In one embodiment, the present invention provides a novel serine **proteinase**, referred to herein as "HELA2" or "testisin", which has roles in spermatogenesis, in suppressing testicular cancer and as a marker for cancers.

L19 ANSWER 19 OF 41 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 2001528613 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11574673
TITLE: Characterisation of PAUSE-1, a powerful silencer in the human plasminogen activator inhibitor type 2 gene promoter.
AUTHOR: Ogbourne S M; **Antalis T M**
CORPORATE SOURCE: Cancer Metastasis Laboratory, Queensland Cancer Fund Experimental Oncology Program, University of Queensland, 4029 Queensland, Australia.
SOURCE: Nucleic acids research, (2001 Oct 1) 29 (19) 3919-27. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011001
Last Updated on STN: 20011029
Entered Medline: 20011025

AB Plasminogen activator inhibitor type 2 (PAI-2) is a serine **protease** inhibitor traditionally regarded as a regulator of fibrinolysis and extracellular matrix degradation. More recently, PAI-2 has been implicated in diverse processes such as keratinocyte differentiation, cell death and viral pathogenesis. The PAI-2 promoter tightly regulates PAI-2 gene expression in a cell-specific manner and this control is mediated, in part, by the upstream silencer element, PAUSE-1. Here we have defined PAUSE-1 and investigated its activity as a silencer. A series of mutations were generated within the PAUSE-1 element and analysed for transcription factor binding and transcriptional silencing activity. These studies have defined the minimal functional PAUSE-1 element as TCTN(x)AGAN(3)T(4), where x = 0, 2 or 4. Examination of related elements present in other promoters, such as the human IFNbeta promoter, suggests that PAUSE-1 is a member of a family of universal silencers with the consensus sequence TCTN(x)AGA. UV crosslinking analyses determined that the PAUSE-1 binding protein was approximately 67 kDa. Insertion of PAUSE-1 into the heterologous (SV40) or the minimal PAI-2 promoters silenced transcription by 2.5-fold. These data show that

PAUSE-1 acts as a powerful silencer of PAI-2 gene transcription and is likely to be important in the silencing of other genes as well.

L19 ANSWER 20 OF 41 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 2001247166 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11231276
TITLE: Organization and chromosomal localization of the murine Testisin gene encoding a serine **protease** temporally expressed during spermatogenesis.
AUTHOR: Scarman A L; **Hooper J D**; Boucaut K J; Sit M L; Webb G C; Normyle J F; **Antalis T M**
CORPORATE SOURCE: The Queensland Institute of Medical Research and the Experimental Oncology Program, University of Queensland, Brisbane, Australia.
SOURCE: European journal of biochemistry / FEBS, (2001 Mar) 268 (5) 1250-8.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF304012; GENBANK-AY005145
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB The recently characterized human serine **protease**, Testisin, is expressed on premeiotic testicular germ cells and is a candidate type II tumor suppressor for testicular cancer. Here we report the cloning, characterization and expression of the gene encoding mouse Testisin, Prss21. The murine Testisin gene comprises six exons and five introns and spans approximately 5 kb of genomic DNA with an almost identical structure to the human Testisin gene, PRSS21. The gene was localized to murine chromosome 17 A3.3-B; a region syntenic with the location of PRSS21 on human chromosome 16p13.3. Northern blot analyses of RNA from a range of adult murine tissues demonstrated a 1.3 kb mRNA transcript present only in testis. The murine Testisin cDNA shares 65% identity with human Testisin cDNA and encodes a putative pre-pro-protein of 324 amino acids with 80% similarity to human Testisin. The predicted amino-acid sequence includes an N-terminal signal sequence of 27 amino acids, a 27 amino-acid pro-region, a 251 amino-acid catalytic domain typical of a serine **protease** with trypsin-like specificity, and a C-terminal hydrophobic extension which is predicted to function as a membrane anchor. Immunostaining for murine Testisin in mouse testis demonstrated specific staining in the cytoplasm and on the plasma membrane of round and elongating spermatids. Examination of murine Testisin mRNA expression in developing sperm confirmed that the onset of murine Testisin mRNA expression occurred at approximately day 18 after birth, corresponding to the appearance of spermatids in the testis, in contrast to the expression of human Testisin in spermatocytes. These data identify the murine ortholog to human Testisin and demonstrate that the murine Testisin gene is temporally regulated during murine spermatogenesis.

L19 ANSWER 21 OF 41 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 2001191926 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11060317
TITLE: Type II transmembrane serine **proteases**. Insights into an emerging class of cell surface proteolytic enzymes.
AUTHOR: **Hooper J D**; Clements J A; Quigley J P; **Antalis T M**
CORPORATE SOURCE: Centre for Molecular Biotechnology, Queensland University of Technology, Gardens Point, Brisbane 4000, Australia.
SOURCE: Journal of biological chemistry, (2001 Jan 12) 276 (2) 857-60. Ref: 67

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

L19 ANSWER 22 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:1194 BIOSIS
DOCUMENT NUMBER: PREV200200001194
TITLE: The serine **protease** testisin functions as a tumor and/or growth suppressor in testicular tumorgenesis.
AUTHOR(S): Boucaut, Kerry Jane [Reprint author]; Douglas, Meaghan L.; Nicol, David L.; Pera, Martin F.; Clements, Judith A.; **Antalis, Toni M.**
CORPORATE SOURCE: CMB, Queensland University of Technology, Brisbane, QLD, Australia
kerryB@qimr.edu.au
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 712. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2001
Last Updated on STN: 25 Feb 2002

L19 ANSWER 23 OF 41 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 2001253397 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11352573
TITLE: Identification and characterization of KLK14, a novel kallikrein serine **protease** gene located on human chromosome 19q13.4 and expressed in prostate and skeletal muscle.
AUTHOR: **Hooper J D**; Bui L T; Rae F K; Harvey T J; Myers S A; Ashworth L K; Clements J A
CORPORATE SOURCE: Centre for Molecular Biotechnology, Queensland University of Technology, Brisbane, Queensland, 4001, Australia.
SOURCE: Genomics, (2001 Apr 1) 73 (1) 117-22.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF283669; GENBANK-AF283670
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20030116
Entered Medline: 20010802
AB The kallikreins are a subfamily of serine **proteases** encoded in human, mouse, and rat by highly conserved tightly clustered multigene families. Here we report the identification and characterization of KLK14, a novel kallikrein gene located within the human kallikrein locus at 19q13.4. KLK14 is approximately 5.4 kb in length spanning seven exons and, by Northern blot analysis, transcribes two alternative transcripts

present only in prostate (1.5 kb) and skeletal muscle (1.9 kb). The protein product, K14, predicted to be a 251-amino-acid secreted serine **protease** with trypsin-like substrate specificity, is translated in vitro with a molecular mass of approximately 31 kDa. In situ hybridization revealed that, in prostate, KLK14 is expressed by both benign and malignant glandular epithelial cells, thus exhibiting an expression pattern similar to that of two other prostatic kallikreins, KLK2 and KLK3, which encode K2 and prostate-specific antigen, respectively.

L19 ANSWER 24 OF 41 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 2001319285 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11391623
TITLE: Human trypsinogen in colorectal cancer.
AUTHOR: Williams S J; Gotley D C; **Antalis T M**
CORPORATE SOURCE: Cancer Metastasis Laboratory, Queensland Institute of Medical Research, Brisbane, Queensland, Australia.
SOURCE: International journal of cancer. Journal international du cancer, (2001 Jul 1) 93 (1) 67-73.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB Trypsinogen (TRY), the precursor to the serine **protease** trypsin, is found in the pancreas and mediates digestive proteolysis in the small intestine. Differential display of cDNAs expressed by human colorectal tumor tissues compared with adjacent normal colonic mucosa identified an isoform of TRY (TRY2) up-regulated in colorectal cancers. Northern blot analysis of RNA isolated from a series of 28 malignant colon tumors and corresponding normal mucosa showed that TRY transcripts were up-regulated 2- to 33-fold in 29% of tumors. Further, TRY mRNA was expressed in 6 colorectal cancer cell lines, with highest levels detected in the metastatic tumor lines SW620 and HT29. Immunostaining for TRY protein expression showed intense immunoreactivity in the supranuclear cytoplasm of colon tumors in 16% of tissue specimens. To evaluate the relative contributions of 2 isoforms of TRY, TRY1 and TRY2, to total TRY mRNA expression, a semi-quantitative multiplex RT-PCR assay was developed. TRY2 mRNA was detected in all 6 colorectal tumor cell lines, whereas TRY1 mRNA was expressed only in the metastatic tumor lines, showing that the high levels of TRY expression in the metastatic tumor lines are likely due to up-regulation of TRY1. Evaluation of TRY1 and TRY2 mRNA expression by multiplex RT-PCR in a series of 20 colon tumor tissues representative of the range of tumor progression showed that TRY2 mRNA was expressed much more commonly than TRY1 mRNA in normal mucosa (26% vs. 6%) as well as in primary tumor tissues (65% vs. 15%). These data demonstrate that TRY2 is the dominant TRY in colon tissue and suggest that up-regulation of TRY1 expression in colon tumors may be associated with a metastatic phenotype.

L19 ANSWER 25 OF 41 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 2001078243 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10969073
TITLE: Tissue-specific expression patterns and fine mapping of the human kallikrein (KLK) locus on proximal 19q13.4.
AUTHOR: Harvey T J; **Hooper J D**; Myers S A; Stephenson S A; Ashworth L K; Clements J A
CORPORATE SOURCE: Centre for Molecular Biotechnology, School of Life Sciences, Queensland University of Technology, Brisbane,

Queensland 4001, Australia.
SOURCE: Journal of biological chemistry, (2000 Dec 1) 275 (48) 37397-406.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB The tissue or glandular kallikreins (KLK) are members of a highly conserved multigene family encoding serine **proteases** that are central to many biological processes. The rodent KLK families are large, highly conserved and clustered at one locus. The human KLK gene family is clustered on chromosome 19q13.3-13.4, and until recently consisted of just three members. However, recent studies have identified up to 11 new members of the KLK family that are less conserved than their rodent counterparts. Using a Southern blot and sequence analysis of 10 BACs and cosmids spanning approximately 400 kilobases (kb) either side of the original KLK 60-kb locus, we demonstrated that these genes also lie adjacent to this. We have also clarified the position of several microsatellite markers in relation to the extended KLK locus. Moreover, from Southern blot analysis of the cosmids and BACs with a degenerate oligonucleotide probe to the histidine-encoding region of serine **proteases**, we have shown that there are no other serine **protease** genes approximately 400 kb centromeric and 220 kb telomeric of the extended locus. We performed an extensive analysis of the expression patterns of these genes by poly(A)(+) RNA dot blot and reverse transcriptase-polymerase chain reaction analysis, and demonstrated a diverse pattern of expression. Of interest are clusters of genes with high prostate (KLK2-4) and pancreatic (KLK6-13) expression suggesting evolutionary conservation of elements conferring tissue specificity. From these findings, it is likely that the human KLK gene family consists of just 14 clustered genes within 300 kb and thus is of a comparable size to the rodent families (13-24 genes within 310 and 480 kb, respectively). In contrast to the rodent families, the newest members of the human KLK family are much less conserved in sequence (23-44% at the protein level) and appear to consist of at least four subfamilies. In addition, like the rat, these genes are expressed at varying levels in a diverse range of tissues although they exhibit quite distinct patterns of expression.

L19 ANSWER 26 OF 41 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 2001097844 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11082206
TITLE: Localization of the mosaic transmembrane serine **protease** corin to heart myocytes.
AUTHOR: **Hooper J D**; Scarman A L; Clarke B E; Normyle J F; **Antalis T M**
CORPORATE SOURCE: Cellular Oncology Laboratory, Queensland Institute of Medical Research, Brisbane, Queensland, Australia.
SOURCE: European journal of biochemistry / FEBS, (2000 Dec) 267 (23) 6931-7.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Corin cDNA encodes an unusual mosaic type II transmembrane serine

protease, which possesses, in addition to a trypsin-like serine **protease** domain, two frizzled domains, eight low-density lipoprotein (LDL) receptor domains, a scavenger receptor domain, as well as an intracellular cytoplasmic domain. In in vitro experiments, recombinant human corin has recently been shown to activate pro-atrial natriuretic peptide (ANP), a cardiac hormone essential for the regulation of blood pressure. Here we report the first characterization of corin protein expression in heart tissue. We generated antibodies to two different peptides derived from unique regions of the corin polypeptide, which detected immunoreactive corin protein of approximately 125-135 kDa in lysates from human heart tissues. Immunostaining of sections of human heart showed corin expression was specifically localized to the cross striations of cardiac myocytes, with a pattern of expression consistent with an integral membrane localization. Corin was not detected in sections of skeletal or smooth muscle. Corin has been suggested to be a candidate gene for the rare congenital heart disease, total anomalous pulmonary venous return (TAPVR) as the corin gene colocalizes to the TAPVR locus on human chromosome 4. However examination of corin protein expression in TAPVR heart tissue did not show evidence of abnormal corin expression. The demonstrated corin protein expression by heart myocytes supports its proposed role as the pro-ANP convertase, and thus a potentially critical mediator of major cardiovascular diseases including hypertension and congestive heart failure.

L19 ANSWER 27 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:238467 BIOSIS
DOCUMENT NUMBER: PREV200000238467
TITLE: Localization, structure and regulation of the human PRSS14 gene encoding the serine **proteinase** testisin.
AUTHOR(S): **Antalis, Toni M.** [Reprint author]; Boucaut, Kerry B. [Reprint author]; Normyle, John F. [Reprint author]; Fitzpatrick, Dave R. [Reprint author]; Hooper, John D. [Reprint author]
CORPORATE SOURCE: Queensland Institute of Med Res, Brisbane, QLD, Australia
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 348. print.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

L19 ANSWER 28 OF 41 MEDLINE on STN DUPLICATE 23

ACCESSION NUMBER: 2000451880 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11004480
TITLE: Localization, expression and genomic structure of the gene encoding the human serine **protease** testisin.
AUTHOR: **Hooper J D**; Bowen N; Marshall H; Cullen L M; Sood R; Daniels R; Stuttgen M A; Normyle J F; Higgs D R; Kastner D L; Ogbourne S M; Pera M F; Jazwinska E C; **Antalis T M**
CORPORATE SOURCE: Cellular Oncology Laboratory, The Queensland Institue of Medical Research, Brisbane, Queensland 4029, Australia.
SOURCE: Biochimica et biophysica acta, (2000 Jun 21) 1492 (1) 63-71.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF058301
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001031

AB Testisin is a recently identified human serine **protease** expressed by premeiotic testicular germ cells and is a candidate tumor suppressor for testicular cancer. Here, we report the characterization of the gene encoding testisin, designated PRSS21, and its localization on the short arm of human chromosome 16 (16p13.3) between the microsatellite marker D16S246 and the radiation hybrid breakpoint CY23HA. We have further refined the localization to cosmid 406D6 in this interval and have established that the gene is approximately 4. 5 kb in length, and contains six exons and five intervening introns. The structure of PRSS21 is very similar to the human prostasin gene (PRSS8) which maps nearby on 16p11.2, suggesting that these genes may have evolved through gene duplication. Sequence analysis showed that the two known isoforms of testisin are generated by alternative pre-mRNA splicing. A major transcription initiation site was identified 97 nucleotides upstream of the testisin translation start and conforms to a consensus initiator element. The region surrounding the transcription initiation site lacks a TATA consensus sequence, but contains a CCAAT sequence and includes a CpG island. The 5'-flanking region contains several consensus response elements including Sp1, AP1 and several testis-specific elements. Analysis of testisin gene expression in tumor cell lines shows that testisin is not expressed in testicular tumor cells but is aberrantly expressed in some tumor cell lines of non-testis origin. These data provide the basis for identifying potential genetic alterations of PRSS21 that may underlie both testicular abnormalities and tumorigenesis.

L19 ANSWER 29 OF 41 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 1999370160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10438806
TITLE: Picornavirus receptor down-regulation by plasminogen activator inhibitor type 2.
AUTHOR: Shafren D R; Gardner J; Mann V H; **Antalis T M**; Suhrbier A
CORPORATE SOURCE: Picornaviral Research Unit, Discipline of Immunology and Microbiology, Faculty of Medicine and Health Sciences, University of Newcastle, Newcastle, New South Wales 2300, Australia.. dshafren@mail.newcastle.edu.au
SOURCE: Journal of virology, (1999 Sep) 73 (9) 7193-8.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990907

AB Therapeutic interference with virus-cell surface receptor interactions represents a viable antiviral strategy. Here we demonstrate that cytoplasmic expression of the serine **protease** inhibitor (serpin), plasminogen activator inhibitor type 2 (PAI-2), affords a high level of protection from lytic infection by multiple human picornaviruses. The antiviral action of PAI-2 was mediated primarily through transcriptional down-regulation of the following virus receptors: intercellular adhesion molecule 1 (ICAM-1, a cellular receptor for the major group of rhinoviruses), decay-accelerating factor (a cellular receptor for echoviruses and coxsackieviruses), and to a lesser extent the coxsackie-adenovirus receptor protein (a cellular receptor for group B coxsackieviruses and group C adenoviruses). Expression of related cell

surface receptors, including membrane cofactor protein and the poliovirus receptor, remained unaffected. These findings suggest that PAI-2 and/or related serpins may form the basis of novel antiviral strategies against picornavirus infections and also therapeutic interventions against ICAM-1-mediated respiratory inflammation.

L19 ANSWER 30 OF 41 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 1999323395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10397266
TITLE: Testisin, a new human serine **proteinase** expressed by premeiotic testicular germ cells and lost in testicular germ cell tumors.
AUTHOR: **Hooper J D**; Nicol D L; Dickinson J L; Eyre H J; Scarman A L; Normyle J F; Stuttgen M A; Douglas M L; Loveland K A; Sutherland G R; **Antalis T M**
CORPORATE SOURCE: Cellular Oncology Laboratory, University of Queensland Joint Oncology Program and Queensland Institute of Medical Research, Brisbane, Australia.
SOURCE: Cancer research, (1999 Jul 1) 59 (13) 3199-205. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 20000303
Entered Medline: 19990728

AB We have cloned and characterized a cDNA encoding a new human serine **proteinase**, testisin, that is abundantly expressed only in the testis and is lost in testicular tumors. The testisin cDNA was identified by homology cloning using degenerate primers directed at conserved sequence motifs within the catalytic regions of serine **proteinases**. It is 1073 nucleotides long, including 942 nucleotides of open reading frame and a 113-nucleotide 3' untranslated sequence. Northern and dot blot analyses of RNA from a range of normal human tissues revealed a 1.4-kb mRNA species that was present only in testis, which was not detected in eight of eight testicular tumors. Testisin cDNA is predicted to encode a protein of 314 amino acids, which consists of a 19-amino acid (aa) signal peptide, a 22-aa proregion, and a 273-aa catalytic domain, including a unique 17-aa COOH-terminal hydrophobic extension that is predicted to function as a membrane anchor. The deduced amino acid sequence of testisin shows 44% identity to prostasin and contains features that are typical of serine **proteinases** with trypsin-like substrate specificity. Antipeptide antibodies directed against the testisin polypeptide detected an immunoreactive testisin protein of Mr 35,000-39,000 in cell lysates from COS-7 cells that were transiently transfected with testisin cDNA. Immunostaining of normal testicular tissue showed that testisin was expressed in the cytoplasm and on the plasma membrane of premeiotic germ cells. No staining was detected in eight of eight germ cell-derived testicular tumors. In addition, the testisin gene was localized by fluorescence in situ hybridization to the short arm of human chromosome 16 (16p13.3), a region that has been associated with allelic imbalance and loss of heterozygosity in sporadic testicular tumors. These findings demonstrate a new cell surface serine **proteinase**, loss of which may have a direct or indirect role in the progression of testicular tumors of germ cell origin.

L19 ANSWER 31 OF 41 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:594236 SCISEARCH
THE GENUINE ARTICLE: 222XP
TITLE: Plasminogen activator inhibitor type-2 (PAI-2) gene transcription requires a novel NF-kappa B-like

transcriptional regulatory motif
AUTHOR: Mahony D; Kalionis B; **Antalis T M (Reprint)**
CORPORATE SOURCE: PO Royal Brisbane Hosp, Queensland Inst Med Res, Brisbane, Qld 4029, Australia (Reprint); Univ Queensland, Brisbane, Qld, Australia; Queensland Inst Med Res, Cellular Oncol Lab, Brisbane, Qld 4006, Australia; Flinders Univ S Australia, Dept Obstet & Gynaecol, Sch Med, Adelaide, SA 5001, Australia
COUNTRY OF AUTHOR: Australia
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (AUG 1999) Vol. 263, No. 3, pp. 765-772.
ISSN: 0014-2956.
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Induction of human plasminogen activator inhibitor type-2 (PAI-2) gene transcription is the response of macrophages to inflammatory stimuli, such as the pleiotropic cytokine, tumour necrosis factor-alpha (TNF alpha). Here we have examined whether PAI-2 gene transcription in response to TNF alpha may be mediated through a regulatory pathway involving the transcription factor, NF-kappa B. We have tested the function of two potential NF-kappa B-like sites present in the PAI-2 proximal promoter for responsiveness to TNF alpha using chloramphenicol acetyl transferase reporter gene deletion and mutation analyses. While no evidence was found for TNF alpha regulation of the PAI-2 gene through either of these two sites, one of the NF-kappa B-like motifs, transcriptional regulatory motif (TRM), present at position -400 was found to be essential for constitutive PAI-2 transcription, as mutation of this motif abolished basal PAI-2 promoter activity in both monocyte-like U937 cells and HT1080 fibrosarcoma cells. Competition electrophoretic mobility shift assays identified four TRM-binding proteins present in U937, HT1080 and HeLa cell extracts, which bound to this motif but were not components of the NF-kappa B regulatory complex. Expression screening of a HeLa cell cDNA library using the -400 TRM as a probe identified two cDNAs encoding partial peptides which specifically bound the TRM motif. DNA sequence analysis revealed that one cDNA was novel, and the second cDNA encoded exon 5 of the nephroblastoma overexpressed (novH) protooncogene, suggesting a new role for this peptide in gene regulation. Taken together, these findings identify a new regulatory element required for constitutive PAI-2 transcription, and identify potential DNA-binding proteins associated with this element that may play a role in PAI-2 gene regulation.

L19 ANSWER 32 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 26
ACCESSION NUMBER: 1999:405519 BIOSIS
DOCUMENT NUMBER: PREV199900405519
TITLE: Testisin, a new human serine **proteinase** expressed by premeiotic testicular germ cells.
AUTHOR(S): Scarman, A. L. [Reprint author]; **Hooper, J. D.** [Reprint author]; Normyle, J. F. [Reprint author]; Nicol, D.; **Antalis, T. M.** [Reprint author]
CORPORATE SOURCE: Cellular Oncology Laboratory, Queensland Institute of Medical Research, Brisbane, QLD, Australia
SOURCE: Biology of Reproduction, (1999) Vol. 60, No. SUPPL. 1, pp. 257. print.
Meeting Info.: Thirty-Second Annual Meeting of the Society for the Study of Reproduction. Pullman, Washington, USA. July 31-August 3, 1999. Society for the Study of Reproduction.

CODEN: BIREBV. ISSN: 0006-3363.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1999
Last Updated on STN: 8 Oct 1999

L19 ANSWER 33 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 27
ACCESSION NUMBER: 1999:184232 BIOSIS
DOCUMENT NUMBER: PREV199900184232
TITLE: The alphavbeta6 integrin induces gelatinase B secretion in colon cancer cells.
AUTHOR(S): Agrez, Michael [Reprint author]; Gu, Xinhua; Turton, Jacqueline; Meldrum, Cliff; Niu, Jun; **Antalis, Toni**; Howard, Eric W.
CORPORATE SOURCE: Discipline Surgical Sci., Faculty Med. Health Sciences, Univ. Newcastle, Callaghan, NSW 2308, Australia
SOURCE: International Journal of Cancer, (March 31, 1999) Vol. 81, No. 1, pp. 90-97. print.
CODEN: IJCNAW. ISSN: 0020-7136.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999
AB In human cancers, the co-operative role between cell-adhesion receptors and **proteases** capable of degrading matrix barriers remains poorly understood. We have previously reported that the epithelium-restricted integrin alphavbeta6 becomes highly expressed in colon cancer compared with normal mucosa and that heterologous expression of alphavbeta6 in colon cancer cells is associated with enhanced cell growth. Herein, we report that alphavbeta6 expression in colon cancer cells leads to a relative increase in secretion of the matrix metalloproteinase gelatinase B over its respective inhibitor and that this secretion parallels the level of cell-surface beta6 expression. The alphavbeta6-mediated gelatinase B secretion is associated with increased proteolysis of denatured collagen at the cell surface, and inactivation of gelatinase B in beta6-expressing tumour cells inhibits cell spreading and proliferation within 3-dimensional collagen matrices. Our findings suggest that alphavbeta6-mediated gelatinase B secretion is important in the progression of human colon cancer.

L19 ANSWER 34 OF 41 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN DUPLICATE 28
ACCESSION NUMBER: 1998-10406 BIOTECHDS
TITLE: New serine **proteases** and kinase involved in regulating cell activity and viability; serine **protease** HELA2 used to regulate cell activity and viability particularly in the testes, for promotion of sperm production, and diagnosis and suppression of cancer, especially testicular cancer
AUTHOR: **Antalis T M; Hooper J D**
PATENT ASSIGNEE: Amrad-Oper.
LOCATION: Richmond, Victoria, Australia.
PATENT INFO: WO 9836054 20 Aug 1998
APPLICATION INFO: WO 1998-AU85 13 Feb 1998
PRIORITY INFO: AU 1997-422 18 Nov 1997; AU 1997-5101 13 Feb 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1998-480768 [41]
AB An isolated proteinaceous molecule (A), e.g. HELA2 (or testin), associated with regulation of cell activity or viability is claimed. (A) is a serine **protease** and can be amplified by the polymerase chain reaction, using the given DNA primers. (A) can also be any protein

with at least 50% identity to the given protein sequences, or encoded by a nucleic acid with at least 50% similarity to the given DNA sequences. Alternatively (A) can be a kinase with a given protein and DNA sequence. Also claimed is a method of regulating cell activity or viability by contacting it with (A). The claims also cover a method of modulating mammal fertility by modulating levels of (A), increasing its levels by introduction of recombinant (A) to facilitate sperm maturation and development. Also covered is a composition containing (A), and an antibody, agonist and antagonist (antisense or ribozyme) capable of interacting with (A). The claims extend to a method of diagnosing cancer or a predisposition to cancer by determining the presence of a sequence encoding (A), as HELA2 is a suppressor of testicular cancer. (167pp)

L19 ANSWER 35 OF 41 MEDLINE on STN DUPLICATE 29
ACCESSION NUMBER: 1998270910 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9607921
TITLE: The serine **proteinase** inhibitor (serpin) plasminogen activation inhibitor type 2 protects against viral cytopathic effects by constitutive interferon alpha/beta priming.
AUTHOR: **Antalis T M**; La Linn M; Donnan K; Mateo L; Gardner J; Dickinson J L; Buttigieg K; Suhrbier A
CORPORATE SOURCE: Queensland Cancer Fund Experimental Oncology Unit, The Queensland Institute of Medical Research, Brisbane 4029, Australia.. toniA@qimr.edu.au
SOURCE: Journal of experimental medicine, (1998 Jun 1) 187 (11) 1799-811.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980713
Last Updated on STN: 20020921
Entered Medline: 19980701

AB The serine **proteinase** inhibitor (serpin) plasminogen activator inhibitor type 2 (PAI-2) is well characterized as an inhibitor of extracellular urokinase-type plasminogen activator. Here we show that intracellular, but not extracellular, PAI-2 protected cells from the rapid cytopathic effects of alphavirus infection. This protection did not appear to be related to an effect on apoptosis but was associated with a PAI-2-mediated induction of constitutive low-level interferon (IFN)-alpha/beta production and IFN-stimulated gene factor 3 (ISGF3) activation, which primed the cells for rapid induction of antiviral genes. This primed phenotype was associated with a rapid development of resistance to infection by the PAI-2 transfected cells and the establishment of a persistent productive infection. PAI-2 was also induced in macrophages in response to viral RNA suggesting that PAI-2 is a virus response gene. These observations, together with the recently demonstrated PAI-2-mediated inhibition of tumor necrosis factor-alpha induced apoptosis, (a) illustrate that PAI-2 has an additional and distinct function as an intracellular regulator of signal transduction pathway(s) and (b) demonstrate a novel activity for a eukaryotic serpin.

L19 ANSWER 36 OF 41 MEDLINE on STN DUPLICATE 30
ACCESSION NUMBER: 1998451511 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9780231
TITLE: DNase I hypersensitive sites in the 5' flanking region of the human plasminogen activator inhibitor type 2 (PAI-2) gene are associated with basal and tumor necrosis factor-alpha-induced transcription in monocytes.
AUTHOR: Mahony D; Stringer B W; Dickinson J L; **Antalis T M**
CORPORATE SOURCE: Queensland Cancer Fund Experimental Oncology Program, The

Queensland Institute of Medical Research, Brisbane, Australia.
SOURCE: European journal of biochemistry / FEBS, (1998 Sep 15) 256 (3) 550-9.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF071400
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981105

AB The plasminogen activator inhibitor type 2 (PAI-2) gene encodes a serine **proteinase** inhibitor (serpin) which is rapidly induced in response to the inflammatory cytokine, tumour necrosis factor-alpha (TNFalpha) in monocytes and macrophages. As an initial step towards understanding the molecular mechanisms underlying PAI-2 gene regulation in monocytes, we report here the analysis of the chromatin structure of 9.6 kb of 5' flanking region of the human PAI-2 gene for potential cis-acting regulatory regions using DNase I hypersensitivity mapping. Sites sensitive to DNase I were mapped in two monocytic cell lines representative of early monocytic differentiation; U937 cells, which synthesise low constitutive levels of PAI-2 that were induced following treatment with TNFalpha, and a MonoMac6 cell line which did not synthesise PAI-2 even after treatment with TNFalpha. Six DNase I hypersensitive sites (DHS) were identified; three upstream of the transcription initiation site (DH1, DH2, DH3) and three downstream of the transcription initiation site which were contained within intron A (DH4, DH5) and the exon 2/intron B junction (DH6). Among these, one distally located DH site (DH2) disappeared in both cell lines following treatment with TNFalpha. Two DH sites (DH1, DH6) were absent in PAI-2-producing U937 cells, but were present in MonoMac6 cells, which did not produce PAI-2, indicating the possible involvement of negative regulatory elements in the suppression of PAI-2 gene expression. The results demonstrate the involvement of chromatin structure in transcriptional responsiveness of the PAI-2 gene promoter and identify several loci which may be key control regions for PAI-2 gene transcription.

L19 ANSWER 37 OF 41 MEDLINE on STN DUPLICATE 31
ACCESSION NUMBER: 1999218572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10200461
TITLE: The C-D interhelical domain of the serpin plasminogen activator inhibitor-type 2 is required for protection from TNF-alpha induced apoptosis.
AUTHOR: Dickinson J L; Norris B J; Jensen P H; **Antalis T M**
CORPORATE SOURCE: Queensland Cancer Fund Experimental Oncology Unit, The Queensland Institute of Medical Research, Brisbane, 4029, Australia.
SOURCE: Cell death and differentiation, (1998 Feb) 5 (2) 163-71.
Journal code: 9437445. ISSN: 1350-9047.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990507

AB The serine **proteinase** inhibitor (serpin), plasminogen activator inhibitor type 2 (PAI-2), has been reported to inhibit tumor necrosis factor-alpha (TNF) induced apoptosis. In order to begin to understand the molecular basis for this protection, we have investigated the importance

of a structural domain within the PAI-2 molecule, the C-D interhelical region, in mediating the protective effect. The C-D interhelical region is a 33 amino acid insertion which is unique among serpins and has been implicated in transglutaminase catalyzed cross-linking of PAI-2 to cell membranes. We have constructed a mutant of PAI-2 wherein 23 amino acids are deleted from the C-D interhelical region generating a structure predicted to be homologous to the closely related, but non-inhibitory serpin, chicken ovalbumin. The PAI-2Delta65/87 deletion mutant retained inhibitory activity against its known serine **proteinase** target, urokinase-type plasminogen activator (uPA); however expression of this mutant in HeLa cells failed to protect from TNF-induced apoptosis. Analyses of the cellular distribution of PAI-2 showed that intracellular PAI-2, and not secreted or cell-surface PAI-2, was likely responsible for the observed protection from TNF-induced apoptosis. No evidence was found for specific cross-linking of PAI-2 to the plasma membrane in either control or TNF/cycloheximide treated cells. The data demonstrate that the PAI-2 C-D interhelical domain is functionally important in PAI-2 protection from TNF induced apoptosis and suggest a novel function for the C-D interhelical domain in the protective mechanism.

L19 ANSWER 38 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 32

ACCESSION NUMBER: 1997:395161 BIOSIS
DOCUMENT NUMBER: PREV199799694364
TITLE: Serine **protease** inhibition and mitochondrial dysfunction associated with cisplatin resistance in human tumor cell lines: Targets for therapy.
AUTHOR(S): Dong, Ying; Berners-Price, Susan J.; Thorburn, David R.; **Antalis, Toni**; Dickinson, Joanne; Hurst, Terry; Qiu, Ling; Khoo, Soo Keat; Parsons, Peter G. [Reprint author]
CORPORATE SOURCE: Queensland Cancer Fund Lab., Queensland Inst. Med. Res., Herston, 4029 QLD, Australia
SOURCE: Biochemical Pharmacology, (1997) Vol. 53, No. 11, pp. 1673-1682.
CODEN: BCPCA6. ISSN: 0006-2952.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1997
Last Updated on STN: 10 Sep 1997

AB Indicators of mitochondrial function were studied in two different cell culture models of cis-diamminedichloroplatinum-II (CDDP) resistance: the intrinsically resistant human ovarian cancer cell line CI-80-13S, and resistant clones (HeLa-S1a and HeLa-S1b) generated by stable expression of the serine **protease** inhibitor-plasminogen activator inhibitor type-2 (PAI-2), in the human cervical cancer cell tine HeLa. In both models, CDDP resistance was associated with sensitivity to killing by adriamycin, etoposide, auranofin, bis(1,2-bis(diphenylphosphino)ethane)gold(I) chloride ((Au(DPPE)-2)Cl), CdCl-2 and the mitochondrial inhibitors rhodamine-123 (Rh123), dequatinium chloride (DeCH), tetraphenylphosphonium (TPP), and ethidium bromide (EtBr) and with lower constitutive levels of ATP. Unlike the HeLa clones, CI-80-13S cells were additionally sensitive to chloramphenicol, 1-methyl-4-phenylpyridinium ion (MPP+), rotenone, thenoyltrifluoroacetone (TTFA), and antimycin A, and showed poor reduction of 1-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), suggesting a deficiency in NADH dehydrogenase and/or succinate dehydrogenase activities. Total platinum uptake and DNA-bound platinum were slightly lower in CI-80-13S than in sensitive cells. The HeLa-S1a and HeLa-S1b clones, on the other hand, showed poor reduction of triphenyltetrazolium chloride (TTC), indicative of low cytochrome c oxidase activity. Total platinum uptake by HeLa-S1a was similar to HeLa, but DNA-bound platinum was much lower than for the parent cell line. The mitochondria of CI-80-13S and HeLa-S1a showed altered morphology and were fewer in number than those of JAM and HeLa. In both models, CDDP

resistance was associated with less platinum accumulation and with mitochondrial and membrane defects, brought about one case with expression of a **protease** inhibitor which is implicated in tumor progression. Such markers may identify tumors suitable for treatment with gold phosphine complexes or other mitochnondrial inhibitors.

L19 ANSWER 39 OF 41 MEDLINE on STN DUPLICATE 33
ACCESSION NUMBER: 96070927 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7499264
TITLE: Plasminogen activator inhibitor type 2 inhibits tumor necrosis factor alpha-induced apoptosis. Evidence for an alternate biological function.
AUTHOR: Dickinson J L; Bates E J; Ferrante A; **Antalis T M**
CORPORATE SOURCE: Queensland Cancer Fund Experimental Oncology Unit, Queensland Institute of Medical Research, Brisbane, Australia.
SOURCE: Journal of biological chemistry, (1995 Nov 17) 270 (46) 27894-904.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19980206
Entered Medline: 19960117

AB Plasminogen activator inhibitor type 2 (PAI-2) is a serine **proteinase** inhibitor or serpin that is a major product of macrophages in response to endotoxin and inflammatory cytokines. We have explored the role of PAI-2 in apoptotic cell death initiated by tumor necrosis factor alpha (TNF). HeLa cells stably transfected with PAI-2 cDNA were protected from TNF-induced apoptosis, whereas cells transfected with antisense PAI-2 cDNA, a control gene, or the plasmid vector alone remained susceptible. The level of PAI-2 expressed by different HeLa cell clones was inversely correlated with their sensitivity to TNF. Loss of TNF sensitivity was not a result of loss of TNF receptor binding. In contrast, PAI-2 expression did not confer protection against apoptosis induced by ultraviolet or ionizing radiation. The serine **proteinase** urokinase-type plasminogen activator was not demonstrated to be the target of PAI-2 action. The P1-Arg amino acid residue of PAI-2 was determined to be required for protection, because cells expressing PAI-2 with an Ala in this position were not protected from TNF-mediated cell death. The results suggest that intracellular PAI-2 might be an important factor in regulating cell death in TNF-mediated inflammatory processes through inhibition of a **proteinase** involved in TNF-induced apoptosis.

L19 ANSWER 40 OF 41 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:50828 BIOSIS
DOCUMENT NUMBER: PREV199598065128
TITLE: Evidence that intracellular plasminogen activator inhibitor type 2 (PAI-2) inhibits a **protease** involved in cell death.
AUTHOR(S): Dickinson, J. L.; Donnan, K.; Linn, M. L.; Suhrbier, A.; **Antalis, T. M.**
CORPORATE SOURCE: Queensland Inst. Med. Res., Brisbane, QLD 4027, Australia
SOURCE: Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 23A.
Meeting Info.: Thirty-fourth Annual Meeting of the American Society for Cell Biology. San Francisco, California, USA. December 10-14, 1994.
CODEN: MBCEEV. ISSN: 1059-1524.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 1995
Last Updated on STN: 1 Feb 1995

L19 ANSWER 41 OF 41 MEDLINE on STN DUPLICATE 34
ACCESSION NUMBER: 88125032 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3257578
TITLE: Cloning and expression of a cDNA coding for a human monocyte-derived plasminogen activator inhibitor.
AUTHOR: **Antalis T M**; Clark M A; Barnes T; Lehrbach P R; Devine P L; Schevzov G; Goss N H; Stephens R W; Tolstoshev P
CORPORATE SOURCE: Biotechnology Australia Pty. Ltd., Roseville, New South Wales, Australia.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1988 Feb) 85 (4) 985-9.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-J03603
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880321

AB Human monocyte-derived plasminogen activator inhibitor (mPAI-2) was purified to homogeneity from the U937 cell line and partially sequenced. Oligonucleotide probes derived from this sequence were used to screen a cDNA library prepared from U937 cells. One positive clone was sequenced and contained most of the coding sequence as well as a long incomplete 3' untranslated region (1112 base pairs). This cDNA sequence was shown to encode mPAI-2 by hybrid-select translation. A cDNA clone encoding the remainder of the mPAI-2 mRNA was obtained by primer extension of U937 poly(A)+ RNA using a probe complementary to the mPAI-2 coding region. The coding sequence for mPAI-2 was placed under the control of the lambda PL promoter, and the protein expressed in Escherichia coli formed a complex with urokinase that could be detected immunologically. By nucleotide sequence analysis, mPAI-2 cDNA encodes a protein containing 415 amino acids with a predicted unglycosylated Mr of 46,543. The predicted amino acid sequence of mPAI-2 is very similar to placental PAI-2 (3 amino acid differences) and shows extensive homology with members of the serine **protease** inhibitor (serpin) superfamily. mPAI-2 was found to be more homologous to ovalbumin (37%) than the endothelial plasminogen activator inhibitor, PAI-1 (26%). Like ovalbumin, mPAI-2 appears to have no typical amino-terminal signal sequence. The 3' untranslated region of the mPAI-2 cDNA contains a putative regulatory sequence that has been associated with the inflammatory mediators.

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(FILE 'HOME' ENTERED AT 16:42:49 ON 13 DEC 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 16:43:14 ON 13 DEC 2005
L1 620411 S PROTEINASE? OR PROTEASE?
L2 394137 S SERINE
L3 104666 S L1 AND L2
L4 9 S "HELA2"
L5 6 DUP REM L4 (3 DUPLICATES REMOVED)

```
L6            2 S L1 AND L5
L7           89 S TESTISIN
L8           80 S L3 AND L7
L9           27 DUP REM L8 (53 DUPLICATES REMOVED)
L10          80 S TUMOR (A)SUPPRESOR
L11      149241 S TUMOR (A)SUPPRESSOR
L12         609 S L3 AND L11
L13          15 S L7 AND L12
L14           6 DUP REM L13 (9 DUPLICATES REMOVED)
                E ANTALIS T M/AU
L15         312 S E3-E7
                E HOOPER J D/AU
L16          90 S E3-E4
L17         377 S L15 OR L16
L18         155 S L1 AND L17
L19          41 DUP REM L18 (114 DUPLICATES REMOVED)
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	L #	Hits	Search Text
1	L1	1	"HELA-2"
2	L2	71969	proteinsae$2 or protease$2
3	L3	27	testisin
4	L4	23	l3 same l2
5	L5	5993	ANTALIS HOOPER
6	L6	573	l2 and l5
7	L7	13	l3 and l6

	Issue Date	Pages	Document ID	Title
1	20030515	104	US 20030092154 A1	Novel molecules

	Issue Date	Pages	Document ID	Title
1	20051117	92	US 20050255558 A1	Novel compounds
2	20051117	72	US 20050255083 A1	Multimeric protein toxins to target cells having multiple identifying characteristics
3	20050818	212	US 20050181375 A1	Novel methods of diagnosis of metastatic cancer, compositions and methods of screening for modulators of metastatic cancer
4	20050728	271	US 20050164343 A1	Novel compounds
5	20040729	31	US 20040146938 A1	Methods of generating and screening for proteases with altered specificity
6	20040520	45	US 20040096915 A1	Methods for detecting ovarian cancer
7	20040513	279	US 20040091969 A1	Novel compounds
8	20040415	337	US 20040072160 A1	Molecular toxicology modeling
9	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
10	20040108	282	US 20040005557 A1	Proteins, polynucleotides encoding them and methods of using the same
11	20031204	73	US 20030224430 A1	Regulation of human eosinophil serine protease 1-like enzyme

	Issue Date	Pages	Document ID	Title
12	20031106	278	US 20030207348 A1	Polypeptides and polynucleotides encoding same
13	20030724	93	US 20030139572 A1	Novel compounds
14	20030703	64	US 20030124579 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
15	20030501	78	US 20030082511 A1	Identification of modulatory molecules using inducible promoters
16	20021010	71	US 20020146407 A1	Regulation of human eosinophil serine protease 1- like enzyme
17	20020404	18	US 20020039753 A1	Method of identifying and treating invasive carcinomas
18	20020124	57	US 20020009730 A1	Human stress array
19	20050308	25	US 6864093 B1	Method of identifying and treating invasive carcinomas
20	20050125	16	US 6846642 B2	Methods of detecting cancer based on prostasin
21	20040316	18	US 6706483 B1	Method of identifying and treating invasive carcinomas
22	20040210	17	US 6689614 B1	Method of identifying and treating invasive carcinomas
23	20030527	19	US 6569684 B2	Method of identifying and treating invasive carcinomas

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1	20051117	92	US 20050255558 A1	Novel compounds
2	20050728	271	US 20050164343 A1	Novel compounds
3	20040513	279	US 20040091969 A1	Novel compounds
4	20031204	73	US 20030224430 A1	Regulation of human eosinophil serine protease 1-like enzyme
5	20030724	93	US 20030139572 A1	Novel compounds
6	20021010	71	US 20020146407 A1	Regulation of human eosinophil serine protease 1- like enzyme
7	20020404	18	US 20020039753 A1	Method of identifying and treating invasive carcinomas
8	20050308	25	US 6864093 B1	Method of identifying and treating invasive carcinomas
9	20050125	16	US 6846642 B2	Methods of detecting cancer based on prostasin
10	20040316	18	US 6706483 B1	Method of identifying and treating invasive carcinomas
11	20040210	17	US 6689614 B1	Method of identifying and treating invasive carcinomas
12	20030527	19	US 6569684 B2	Method of identifying and treating invasive carcinomas

13	20021112	99	US 6479274 B1	DNA molecules encoding human HELA2 or testisin serine proteinases